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THE FUNCTIONAL POINT OF VIEW IN RHINOLOGY

CHAIRMAN'S ADDRESS

ARTHUR W. PROETZ, M.D.

ST. LOUIS

When a man sets out to tinker with an alarm clock one of two things is almost certain to happen: Either he gets it going or he has enough parts left over to make a wrist watch, and neither of them runs or ever will. The result does not depend on his virtuosity with a screwdriver nor does it rest on his knowledge of radio, firearms or locomotives. If he succeeds in putting it in order it is only because he understands how clocks work.

So it is with the nose. To deal successfully with a nose the rhinologist must understand the basic principles of surgery, to be sure. Granted he must be skilful with his hands. He must be conversant with the local anatomy. But above all he must know how a nose works.

Until recently he has unexplainably paid little attention to function. Many a monograph and many a textbook have been written on the nose with never a word about its physiology. Many an operation has failed of its purpose because the surgeon had not clearly in mind how or even whether it might accomplish what he intended it to.

The reason for his long protracted indifference is not clear. Most of what he knew—or thought he knew—about nasal physiology had been discovered by some one not vitally interested in the nose. It was often the by-product of an investigation far removed from the problems of rhinology. It was not infrequently deduced from the observations of zoologists working with tissues not human but from animals whose habitats, environments and genealogies are wholly unlike our own.

Any one who attempts to prepare a course of lectures to advanced students on the physiology of the nose cannot fail to be dismayed at the scarcity of material available. From the indexes he may gather many titles scattered through the literature of the past fifty years, but he will be disappointed in the sum total of factual information.

Whether this is the cause or the effect of a widespread preoccupation with other problems on the part of our immediate predecessors is of no great moment. The fact remains that the authors of all but a very few textbooks have contented themselves with the mere mention of matters physiologic—usually a few introductory paragraphs, lost among the descriptions of head mirrors and office equipment—and then have proceeded, with never a backward glance, to describe and endorse procedures which plainly showed that they still regarded the nose as only a distressingly tortuous air passage and nothing more. This misconception led to much futile therapy.

It resulted, for example, in the failure to differentiate surgically between a sinus empyema and an abscess. Even contemporary textbooks seldom point out that a pus filled nasal accessory cavity is essentially a space, an air cell, of proportions and relations important to its health, with sensitive functioning mechanisms, while an abscess is not a space at all but a collection of pus, rending tissues apart and creating, only after its evacuation, a cavity where no cavity has any business to be. To regard these two surgically as one and the same thing is a blunder responsible for much lingering distress.

It resulted further in a disregard for nasal tissues as such. Not so long ago it was widely taught that no special requirement was met by conserving them, that they could be sacrificed fairly promiscuously, merely for the surgeon's momentary convenience. No mention was made of air currents thus misdirected against some sensitive area of the upper nose, producing intractable headaches. Subsequent crusting was attributed not to the resulting dryness but to incomplete eradication, and more and more was done—instead of less and less—for the point of view was structural instead of functional.

These things are of the past—just barely. Ten years ago, before one of the national societies then meeting in San Francisco, I called a speculum a spade and inveighed against our indifference to the intimate workings of the nose.

Today my tirade would lack point. I am happy to say that the recrudescence of interest in nasal physiology has been due largely to the investigations of Americans. There have been repercussions in England, in Germany and particularly in the North Countries. It is encouraging that a purely physiologic subject was at last selected for official discussion by the fourth International Congress of Otolaryngology, to have been held next month in Amsterdam but now regrettably postponed. It is notable that the new work has, for the first time, come almost exclusively from the laboratories of rhinologists actively engaged in clinical work. On the whole it is based on experimental evidence of a quality which entitles it to our respectful attention.

It is the part of the clinician to apply such available knowledge intelligently to the individual case and to avoid routines which in industry may be the index of efficiency and production but in science are the graveyards of progress.

The application of new knowledge is twofold: To heed what has been done in the laboratory and to apply it wisely to the patient: to adopt new methods, new drugs, new operations intelligently is progress. It is likewise progress, though it seldom occurs to us, to

Read before the Section on Laryngology, Otology and Rhinology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

abandon old methods, old drugs and old operations when they have been discredited. Not to abandon them after they have been proved harmful is reprehensible.

One is constantly confronted with the need of a critical evaluation of methods. I shall not enlarge on this, as the therapeutic "how" and "why" will presently be threshed out on this floor. I wish only to point out that the functions of the nose, whatever they may ultimately prove to be, have a vital influence on the air we breathe. What could be more important?

I wish to add that it is not enough to maintain breathing channels but that the mechanisms by which the nose keeps itself clean must be conserved or restored if it is to continue functioning and maintain its possessor in comfort. It is not enough to know that quantities of moisture are required to saturate inspired air unless we act on that knowledge by conserving and cultivating the humidifying equipment of the mucosa, already often taxed to the limit by the droughts of central heating. It is not enough to know that air currents are evenly distributed over the streamlined contours of the nasal fossae without being keenly aware that they may not be misdirected with impunity. I will not labor the point.

Little by little, as the physiology of the nose is better understood, therapeutic and surgical methods will conform to it; but in the meantime it behooves us individually to find out more about how our alarm clock works before we begin throwing away any of the wheels.

3720 Washington Boulevard.

USE OF BISMUTH INJECTIONS TO MANAGE COURSE OF THERAPEUTIC MALARIA

HAROLD N. COLE, M.D.
GERARD A. DEOREO, M.D.
JAMES R. DRIVER, M.D.
HERBERT H. JOHNSON, M.D.
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PASADENA, CALIF.

Malaria is being used more and more in the treatment of resistant syphilis of the central nervous system as well as of dementia paralytica. This form of fever treatment has established its value in spite of the definite risk associated with it, even in selected cases. For this reason there is a growing need for some means of management of therapeutic malaria. Thus, if some agent were at hand to cause a temporary interruption in the course of the fever for even forty-eight hours, there would be an opportunity for the patient to recover from the effects of the fever. The cycle might then be allowed to continue until sufficient hours of hyperpyrexia had been accomplished.

In 1937 Fong [1] reviewed the literature on malaria mortality and reported eleven series of cases, totaling 13,267 patients. In this group, in part unselected, the mortality was 7.51 per cent. The usual causes of death were physical exhaustion, kidney and liver insufficiency, and vascular collapse. With the exception of the last condition, death was as a rule not sudden; usually ultimate failure was heralded in ample time so that some form of supportive measure (malaria management) could have been used had it been available. It is for these untoward reactions in the course of malaria therapy that the use of thio-bismol is offered.

USE OF HEAVY METALS IN THE TREATMENT OF MALARIA

The value of preparations of bismuth and other heavy metals in the treatment of epidemic malaria has been mentioned by various writers. Speranza [2] has reported on the use of bismuth; Sanyal [3] and deNunno [4] have spoken of the value of antimony in treating quinine-resistant malaria; Gualdi [5] has observed the action of gold, and Ross,[6] Liu,[7] deMello and Vernencar,[8] Peroni [9] and Bird [10] have used mercury in combating the disease. Various arsenical preparations have been employed by Goldman,[11] Cleveland and Turvey,[12] Young and McLendon,[13] Solomon, Epstein and Berk,[14] Tardres,[15] Sinton,[16] Murphey [17] and many others.

In May 1938 one of us [18] reported the effect of thiobismol (bismuth sodium thioglycollate) in twenty-one cases of malaria at Cleveland City Hospital. Of this series nineteen were an artificial asexual strain (used in the treatment of central nervous system syphilis) and two were naturally acquired tertian malaria. Since this original report, 129 patients from the Dermatology and Syphilology Services of City and of the University Hospitals have been studied. This included some 150 observations on bismuth and other heavy metals. Each patient had received an intravenous inoculation of malarial blood (from 2 to 5 cc. with no attempt as to type compatability) and had every evidence of the disease. This strain has been kept alive for sixteen

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Read before the Section on Dermatology and Syphilology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

From the Department of Dermatology and Syphilology, Cleveland City Hospital, the University Hospitals, and Western Reserve University Medical School.

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17. Murphey, E. E.: Use of Sodium Cacodylate in Malaria, J. M. A. Georgia **16**: 20-24 (Jan.) 1927; Sodium Cacodylate in Pernicious Malaria, South. M. J. **22**: 363-366 (April) 1929.

18. Schwartz, W. F.: Effect of Thio-Bismol on Therapeutic Malaria, J. Pharmacol. & Exper. Therap. **65**: 175-184 (Feb.) 1939.

years by transinoculation from patient to patient and has lost none of its original vigor. Of this number 103 patients were given thio-bismol to manage the course of the therapeutic fever, and in addition to other soluble and insoluble bismuth preparations various compounds of antimony, mercury, arsenic and gold were employed. Further, sodium thioglycollate,[19] the vehicle of thio-bismol (bismuth sodium thioglycollate) was tried to determine whether it played a part. This was done in order to make sure that it was the bismuth rather than the thioglycollate that had the antimalarial effect. In the process a few related heavy metals were only casually examined.

Antimony.—Fuadin, a brand of stibophen (sodium antimony biscatechol disulfonate of sodium), antimony and potassium tartrate and sodium antimony thioglycollate were employed.

Fuadin.—Only five patients were in this group. Doses of 1.5 and 2 cc. were ineffective, so a larger dose was tried. The results in all cases were uniform, so description of one typical reaction will suffice. The patient had excellent elevations every forty-eight hours. After the fourth chill, 3 cc. of fuadin was given intramuscularly and an additional 3 cc. was given intravenously. The malaria terminated and the patient was then carried on typhoid injections as a substitute. He was in the hospital for twenty-five days without a single spontaneous rise of temperature. On two occasions rare plasmodia were found in the peripheral blood after injection of epinephrine.

Antimony and Potassium Tartrate.—Observations were made on but two patients. One patient was given 0.05 Gm. in a 1 per cent solution intravenously before the seventh paroxysm was anticipated (this elevation came unaltered 40.7 C., or 105.3 F.) and 0.075 Gm. of the drug was given just before the eighth chill. This chill was reduced to 40 C. (104 F.) and no further paroxysms followed. Frequent blood examinations were made for parasites and only after injection of epinephrine (1 cc. subcutaneously) were any parasites found in eight days of observation. The second case was similar to this one.

Sodium Antimony Thioglycollate.—Two patients who were chilling were given 20 cc. of a 0.4 per cent solution intravenously. In each the chills were terminated, one for four days and one for five days, after which the cycle was resumed.

Extended study of antimony compounds may reveal a preparation suited to temporary checking of a therapeutic malaria course. The ones examined either stopped it entirely or had an effect unsuitable for our purpose.

Arsenic.—Arsphenamine, neoarsphenamine and mapharsen have been used for years either as a means of "slowing" the course of malaria or in combination with quinine in the attempt to terminate the fever when that drug alone has failed. There is no doubt that they have an antimalarial effect. However, it is not a reliable method of producing a "rest period" from the chills, since often a single injection fails to produce the desired result, or it may terminate the course of the fever entirely. Recent observations in additional cases were consistent with former experience and with the experience of others.

19. Ampules of sodium thioglycollate were furnished by Parke, Davis & Co. for this study.

Mercury.—Salyrgan was used on three patients. Three injections of 2 cc. each were given on alternate days without any change in the subsequent course of the fever. Parasites were found in the blood stream without difficulty.

With mercuric succinimide, one patient was given 0.01 Gm. every day for ten days during the course of malaria without any alteration in the type of cycle or in the intensity of paroxysms. To another patient through error was exhibited 0.012 Gm. every six hours for five injections without any change.

Gold.—Gold sodium thiosulfate was used on two patients, the first receiving 10 mg. intravenously and the second 25 mg., without any effect.

Sodium Thioglycollate.—This preparation is the vehicle in which thiobismol is given, and it was administered to seven patients in doses exceeding that found in the usual injection of thio-bismol. There was no effect, even after long observation periods. Evidently the thioglycollate radical does not play a main role in the effect of thio-bismol on therapeutic malaria.

Bismuth.—Bismuth subsalicylate has been used for years almost as a routine throughout the course of malaria. A review of many of these charts shows no constant change in the course of the malaria which could be attributed to this drug. It may be that some of the "spontaneous terminations" seen occasionally were the result of this cumulative bismuth action, but unexplained termination of malaria is also seen when no bismuth is employed.

Both the oral and intramuscular preparations of sobisminol have been used. One patient, chilling every forty-eight hours (average temperature elevation of 40 C.), who had had nine paroxysms, was given three capsules (0.75 Gm., each 0.15 Gm. of metallic bismuth) three times daily for seven days. After the second day the temperature rose to 39 C. (102.2 F.) and fluctuated between 38 and 39 C. (100.4 and 102.2 F.) for the next seven days, then dropping to normal for seven days before quinine was instituted. Parasites were found during the first seven day period but none were found later. A 2 cc. intramuscular injection of sobisminol (0.04 Gm. of metallic bismuth) was given during each of the fifth, sixth and seventh chills. They were reduced in severity, but subsequent temperature rises regained the original level.

Biliposol (2 cc. contains 0.08 Gm. of bismuth), a liposoluble compound which should give a very high bismuth level in the blood stream, was used in three cases. In the first case three daily injections were given. The patient had one chill after the last injection (his sixth chill) and there were no subsequent chills for a period of thirty-two days, during which time the patient was receiving typhoid vaccine. No parasites were found on repeated blood smears. In the second instance four daily injections of the drug were given after the patient had completed his fourth daily chill. The fifth chill was unaltered but the sixth and seventh were reduced in intensity, and no additional paroxysms were observed in the following fifteen days during which time typhoid vaccine was used. However, it was possible to demonstrate an occasional malarial organism in the peripheral blood during the observation period. Results were not satisfactory for the end desired.

Sodium bismuth tartrate was given to four patients in injections of 4 cc., since 2 cc. apparently had no effect. Two patients received two daily treatments, one

received three and the last received four. In no instance was any appreciable change produced.

Bithoxyl (an experimental liposoluble compound in which each cubic centimeter contains 0.06 Gm. of bismuth) was used for seven observations. Two patients received two 2 cc. injections, two received three, two more five, and another six. The first four patients (those receiving two and three injections respectively) showed no change in the course of the malaria. In the last three (receiving five and six daily injections respectively) the malaria was interrupted for the periods of observation, four, seven and twelve days respectively.

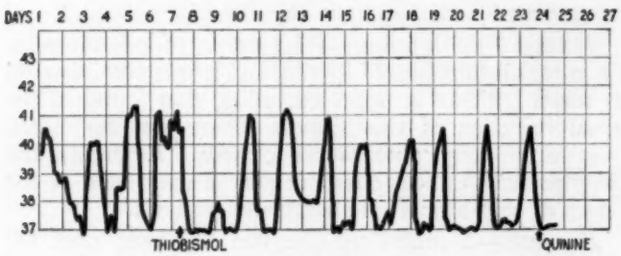

Chart 1.—Rest period provided in tertian cycle by single injection of thio-bismol 0.2 Gm.: Number of observations, seven cases. Rest period with reversion to tertian cycle, five cases: Failures: permanent cessation, one case; no effect, one case. Percentage of satisfactory results, 71.43.

No parasites were found in any case. Results were inconclusive for the effect desired.

Iodobismitol was used in eight instances. Two of the patients were given the drug before and during the incubation period after malarial inoculation; these patients did not take. In the remaining six the medication was used after the cycle had been established and from nine to eleven days after the bismuth had been started (the patients having had from three to six chills) the paroxysms ceased for observation periods varying from five to twenty-one days.

Thio-bismol was used in 103 observations, ninety-two of them with a single injection and eleven with more than one injection. The dose employed was the routine intramuscular 0.20 Gm. In general there were three types of malarial cycles in which it was used. The early prolonged prodromal remittent rise was encountered in from one third to one half of the patients inoculated intravenously; there was a second group in which a double cycle was encountered; finally there was a smaller group in which the fever originally assumed a tertian cycle. By far the greatest usefulness of thio-bismol is found in its effect on the prolonged remittent temperature rise and in the double tertian type of cycle. Moreover, it is in these groups of patients that untoward effects from the fever therapy are most common.

POSSIBLE RELATION OF ABSORPTION AND EXCRETION OF THIO-BISMOL TO THE PROBLEM

Thio-bismol is rapidly assimilated and excreted. Sollmann, Cole and their co-workers have shown that an injection of the drug is virtually absorbed and excreted within twenty-four hours. Thio-bismol is sodium bismuth thioglycollate $Bi(SCH_2CO_2Na)_3$ and contains approximately 38 per cent of bismuth. The average 0.20 Gm. intramuscular dose contains 75 mg. of metallic bismuth. It has been shown [20] that the bismuth level in the blood stream as measured by urinary excretion reaches a very high level within a matter of hours and then even as rapidly drops. Perhaps this may explain why some bismuth preparations have little or no effect on Plasmodium vivax. They do not reach this high level, transitory it is true, in such a short time.

RESULTS FROM INJECTION OF THIO-BISMOL

The value of the thio-bismol injection is in temporarily arresting the course of the therapeutic malaria. A single injection of this drug given just before a chill will bring about nearly always within six to twelve hours a rest period from the fever. The change produced in the type of chill which is to follow depends on the type of cycle which was present when the medication was given.

Prolonged Remittent Fever.—A forty-eight hour respite is the rule if the patient is suffering from a prolonged, tiring, constant, febrile attack. If untreated, this type may occasionally persist for eight or even ten days, if the patient does not succumb before that. During this respite the patient is afebrile, has none of the symptoms associated with the febrile phase of the disease and is able to take nourishment and important fluids that he could not formerly retain. After a two day rest the paroxysms return on alternate days (chart 1).

Daily Cycle.—If, on the other hand, the patient is chilling daily (double tertian) a single injection of thio-bismol will again remove one of the cycles so that a forty-eight hour rest period is provided and the patient continues to chill, not every twenty-four hours but every forty-eight hours (chart 2).

Alternate Cycle (Tertian).—When an injection of thio-bismol is given to a patient chilling every forty-eight hours, the results are not so predictable. Usually (if it is given early in the course of the malaria) only one chill is eliminated, giving an additional forty-eight hours rest. Then the cycle continues. If the drug is given more than ten hours before the next expected chill (by which time the drug will have been excreted) no effect is observed (chart 3). Rarely a single injection will terminate the clinical malaria entirely, though parasites may be found in the blood after stimulation with epinephrine. The apparently inconsistent reactions to thio-bismol in this group are readily understandable when one remembers the rapidity with which the drug is excreted. The bismuth is almost entirely eliminated within twenty-four hours and the blood therapeutic level has been exhausted hours before that. Hence there may be no appreciable number of parasites in the blood stream at the time the bismuth is at a therapeutic level. This is not true in the first two groups of patients, for here the chills are persistent or occur every twenty-four hours.

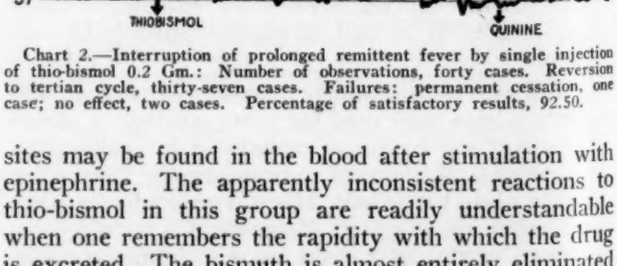

Chart 2.—Interruption of prolonged remittent fever by single injection of thio-bismol 0.2 Gm.: Number of observations, forty cases. Reversion to tertian cycle, thirty-seven cases. Failures: permanent cessation, one case; no effect, two cases. Percentage of satisfactory results, 92.50.

20. Sollmann, Torald; Cole, H. N.; Henderson, Katharine; Binkley, George W.; Connor, W. H., and Sullivan, Maurice: Clinical Excretion of Bismuth: II. The Urinary Excretion of Bismuth After Clinical Intramuscular Injections of Sodium Iodobismuthite (Sodium Bismuth Iodide, Iodobismitol) and Sodium Bismuth Thioglycollate (Thio-Bismol), Am. J. Syph., Gonor. & Ven. Dis. **21**: 480 (Sept.) 1937.

VALUE OF THE THIO-BISMOL CONTROL OF THERAPEUTIC MALARIA

Before we were acquainted with the action of thio-bismol, patients in an unfavorable condition were deprived of an opportunity to continue malaria therapy, as quinine usually terminated the course. It was very difficult to work out a dose that would temporarily stop the chills. Or if the patients were allowed to continue having paroxysms in spite of unfavorable clinical or laboratory evidence, serious, even fatal, complications were too common results. Through the use of thio-bismol the cycle can be altered, giving the patient a one or two day rest period in which to recuperate. Usually this interval is sufficient so that the patient may then be allowed to resume a further cycle and continue until there has been a sufficient number of therapeutic chills. If, however, the respite has not been enough to bring this about and the condition of the patient is still precarious, quinine can then be given to terminate the malaria completely.

Effect of Single Injection of Thio-Bismol on Therapeutic Malaria

A. Effect on prolonged remittent fever:	40 cases
1. Rest period of 48 hours with reversion to tertian cycle..	31
2. Temporary interruption for 3 to 5 days with reversion to tertian cycle	6
3. Permanent cessation	1
4. No effect	2
B. Effect on double tertian cycle:	45 cases
1. Rest period of 48 hours with reversion to tertian cycle..	38
2. Temporary interruption of 3 to 5 days with reversion to tertian cycle	6
3. Permanent cessation	1
C. Effect on tertian cycle:	7 cases
1. Temporary interruption of 3 to 5 days with reversion to tertian cycle	5
2. Permanent cessation	1
3. No effect	1

Usually the rest period is sufficient to allow recovery from (1) prolonged exhausting fever, (2) weakness and prostration, (3) impending vascular collapse, (4) protracted vomiting, (5) rapidly developing anemia, (6) increasing icterus, (7) rapidly rising blood urea nitrogen.

The table shows that in forty cases of prolonged remittent fever after a single injection of the thio-bismol a rest period of plus or minus forty-eight hours resulted in thirty-one cases, and there was a temporary interruption for from three to five days in a further six cases. In forty-five cases of double tertian malaria a single injection caused a rest period for plus or minus forty-eight hours with reversion to the tertian cycle in thirty-eight cases and a temporary interruption of from three to five days in a further six cases. In seven cases on the tertian cycle there was a temporary interruption of from three to five days in five cases. In the entire ninety-two cases there were but four cases with no effect after the single injection of thio-bismol.

CASE STUDIES

Presentation of three typical cases will demonstrate the results of therapeutic malarial control by thio-bismol:

CASE 1.—E. B., a woman aged 30, with a diagnosis of paresis sine paresi, had an initial prolonged remittent type with daily temperature elevation varying from 40.5 C. to 41.6 C. (from 104.9 to 106.4 F.) and not dropping to normal for a period of six days. At this time she showed evidence of prostration. She took little food or water and vomited what little she had taken. The blood urea nitrogen (which had been normal at the onset) rose rapidly to 40 mg. per hundred cubic centimeters. An injection of thio-bismol (0.2 Gm.) was given. Within eight hours the temperature had dropped to normal and remained so for the next forty-eight hours. This respite was sufficient to allow the patient to gain the rest and nourishment she needed. Blood urea nitrogen fell to 21 mg. per hundred cubic centimeters and the patient was deemed strong enough to continue. As expected, the chills resumed spontaneously after forty-eight hours and chills of a good intensity, from 40 to 41.4 C. (104 to 106.5 F.) proceeded at regular forty-eight hour intervals. The patient was allowed to have six additional chills (total twelve) without further difficulty. The blood urea nitrogen was down to 12 mg. per hundred cubic centimeters after the twelfth paroxysm.

CASE 2.—A. V., aged 64, with a diagnosis of early dementia paralytica, had been chilling on alternate days for three paroxysms. The fourth elevation remained at a persistent level of 41 C. (105.8 F.) for two days; during this time there was evidence of exhaustion; the blood urea nitrogen was 16.6 mg. per hundred cubic centimeters and the icteric index was 14 units. The usual dose of thio-bismol was given. The temperature returned to normal in seven hours and remained so for the next forty-eight hours. There was immediate improvement and the patient tolerated eight more much needed malarial bouts, which came spontaneously every forty-eight hours. At the end of the desired course of hyperpyrexia the blood urea nitrogen was normal, 11.2 mg. per hundred cubic centimeters, and the icteric index was 7 units.

CASE 3.—J. A., a man aged 48, with a diagnosis of dementia paralytica, was having severe daily chills, the temperature reaching 41 C. (105.8 F.) and maintaining the level for from eight to ten hours. During the fifth such cycle the patient showed signs of physical exhaustion and of vascular collapse. He was unable to take anything by mouth. There was a profound delirium and a falling blood pressure, 84 systolic, 40 diastolic. Thio-bismol was injected intramuscularly and the temperature fell to normal in six hours. The blood pressure responded, returning to 110 systolic and 60 diastolic, the sensorium became clear, and in general his condition was again quite good. After forty-eight hours the sixth chill came on spontaneously and he continued to have alternate paroxysms until he had received a total of eleven good reactions, at which time quinine was started. The blood chemistry showed but little change throughout the entire course of treatment.

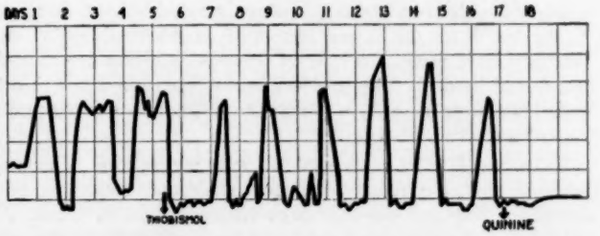

Chart 3.—Double tertian infection changed to tertian by single injection of thio-bismol: Number of observations, forty-five cases. Reversion to tertian cycle, forty-four cases. Failure: permanent cessation, one case. Percentage of satisfactory results, 97.77.

OTHER EFFECTS OF THIO-BISMOL

The main purpose of this study was to learn a method of managing therapeutic malaria without stopping the fever altogether, so that the value of the therapeusis would not be lost. However, it is worth mentioning briefly other actions of thio-bismol in malaria. Many times a patient will have one or even two additional chills after quinine therapy has been instituted to end a course of malaria. Most of the time this is not undesirable, but occasionally this added chill may be more than the patient can tolerate. To prevent this thio-bismol is given and quinine started at the same time.

The thio-bismol will eliminate the next expected chill and by that time the quinine has become effective. This procedure is especially valuable if the patient is vomiting. Another method of preventing "added" chills, when it is desirable to stop the malaria, is the use of repeated daily injections of thio-bismol. With three daily injections it was found that paroxysms were terminated for periods varying from five to thirty-nine days before quinine was given. Further, in the unusual instance when the disease is resistant to ordinary antimalarial drugs (quinine or atabrine) the use of thio-bismol along with these drugs seemed to enhance their antimalarial properties, as was found in two quinine resistant malarias of the asexual strain.

RESULTS OF THIO-BISMOL TREATMENT

In the period of time since we have been employing thio-bismol to alleviate the effects of therapeutic malaria, 263 patients have been treated in our wards. It is true that our cases are in part selected in type. It is not possible to handle advanced mental cases in the service. Some of our patients, however, are quite degenerated and by no means good risks. During this period our mortality rate has been 2.24 per cent. There were six deaths, one from heat exhaustion, three from cerebral thrombosis, one from pyelonephrosis in a patient with a horseshoe kidney, and one from spontaneous rupture of the spleen. Moreover, as a result of the beneficial effects of the thio-bismol our patients almost without exception have been able to take a full complement of fever treatments, something that would have been impossible in the past.

The following two cases illustrate what may occur in any ward where this drug is not employed to take full advantage of malarial therapy. Both patients were treated with the same strain of benign tertian parasite that is being used today. These two patients were treated just before Schwartz had found the value of thio-bismol, and it is interesting to conjecture as to the ultimate outcome had thio-bismol been employed:

CASE 4.—A. B., a man aged 44, with a diagnosis of dementia paralytica, was chilling daily. By the time he had had seven paroxysms, the blood urea nitrogen had risen to 42 mg per hundred cubic centimeters. Intravenous dextrose, parenteral fluids and 5 cc. of 10 per cent quinine dihydrochloride intravenously were given. In spite of this his condition grew steadily worse and he died. The problem in this instance seems to differ very little from case 3, in which thio-bismol was given and the patient survived.

CASE 5.—F. G., a man aged 40, with a diagnosis of dementia paralytica, had a long, persistent prodromal elevation, which lasted for five and one-half days (from 39.8 to 40 C., or 103.6 to 104 F.). At the end of this time his condition was not grave, but progress notes indicated that fluids and food were refused and the patient was "very restless." After four additional chills the patient showed signs of impending vascular collapse, and supportative measures were given. Quinine urea hydrochloride 0.5 Gm. was given intramuscularly and quinine sulfate 10 grains (0.65 Gm.) was given by mouth. The patient did not respond to this, the temperature failed to drop, and he died. Case 1 of our series was much like this case and responded to thio-bismol.

COMMENT

The question naturally arises whether this peculiar action of thio-bismol is truly antimalarial. Such apparently is the case. Further, it is difficult to explain the selective action on alternate cycles of malaria unless on the basis that the drug acts most on that set of parasites which are at a certain stage of maturation.

It seems fair to conclude that the bismuth itself is the responsible component for the antimalarial action of thio-bismol. The vehicle of the preparation (sodium thioglycollate) was given in doses as large and even exceeding the amount given in the usual dose of thio-bismol, and it produced no effect whatever on the malaria. In fact, this study has been confined mostly to thio-bismol, and it is quite possible that further investigation will reveal other bismuth preparations that will have even as great an effect in therapeutic (asexual) malaria. After all, some of our observations with other compounds were not in sufficient number to be statistically of value. Shortly after an injection of thio-bismol there is a rapid but transitory high level of bismuth in the blood stream. It is quite possible that this high level as measured in terms of urinary excretion may explain the value of the drug in this particular situation.

SUMMARY

1. Therapeutic malaria employed in the treatment of central nervous system syphilis sometimes leads to one or more of the following alarming symptoms: (*a*) prolonged remittent fever, (*b*) physical exhaustion, (*c*) vascular collapse, (*d*) persistent vomiting, (*e*) an increasing anemia, (*f*) rapidly rising icteric index, (*g*) rapidly rising blood urea nitrogen.

2. If an agent could be found that would temporarily stop the course of the malarial chills, with rest thus furnished, it might be possible then to continue the chills to a satisfactory completion of the course.

3. Studies made with various selected heavy metals indicate that, while antimony compounds may in part satisfy this demand, certain bismuth salts, and more particularly thio-bismol, answer the requirements.

4. In the one to three day rest period from the chills, the fever drops, exhaustion, vascular collapse and persistent vomiting disappear, the blood urea nitrogen and the icteric index fall, the blood pressure rises to more normal levels, and with resumption of the chills the patient's increased strength allows him to go on to a completion of his course of chills.

5. The action of the thio-bismol and of other bismuth salts seems to be a bismuth effect on the malarial parasite. Its success may depend on the rapid attainment following the bismuth injection of a high transitory bismuth level in the blood stream as measured in terms of bismuth excretion in the urine.

6. Repeated injections of bismuth, especially thio-bismol, stopped therapeutic malaria for long observation periods (as long as thirty-nine days).

7. It is not to be assumed that we offer thio-bismol as a substitute for quinine in terminating malaria, but we do maintain that thio-bismol is a reliable drug in the management of therapeutic malaria and by its use many untoward therapeutic malarial results can be avoided.

8. Moreover, where it is desired to terminate a course of therapeutic malaria without shock to the patient, it will be found that an intramuscular injection of thio-bismol plus quinine or atabrine by mouth will accomplish this.

9. With the use of thio-bismol as indicated in 263 cases of therapeutic malaria in our wards, the death rate was 2.24 per cent. Moreover, with the help of the drug it was possible to carry on the course of malaria until the patients had had an adequate number of hours of hyperpyrexia.

ABSTRACT OF DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: A survey of the value of mechanotherapy and malaria therapy by a group interested in both types of fever therapy was recently completed. The parallelism in both the therapeutic results and the serologic results was striking in a group of patients with dementia paralytica treated and observed for more than five years. Therapy by mechanical means has a few advantages and malarial therapy likewise has a few advantages, but it was obvious that the outstanding disadvantages of malaria were the points that the authors have called attention to, namely exhaustion, debility and anemia. It has been the inability heretofore to control the intensity of the malarial reactions satisfactorily that has justified some criticism of this type of fever therapy. Thiobismol as a modulator of malaria therapy has greatly reduced the intensity and severity of these reactions. Dr. Cole suggested the value of thiobismol as a modulator to me and during the past few months I have given it to thirty out of ninety patients undergoing malaria therapy. The "comeback" following an injection of thiobismol of the individual who has become exhausted and debilitated from the malaria course is striking. It has been my experience that in the small individual who weighs less than 115 or 120 pounds (about 53 Kg.) it is advisable to use less than 1 cc. of the thiobismol. I observed one patient who went for eight days without chills or fever following the thiobismol and whom it was necessary to reinoculate with Plasmodium vivax; in other words, to reinduce the malaria. I do not mean to imply that thiobismol is curative as regards malaria, but the drug ameliorated the infection to the point that it was necessary to reinoculate her and start the fever course again. I do not know what influence thiobismol will have on the clinical and serologic results from malaria therapy. I cannot imagine that it will influence the results of this type of fever therapy in any way whatever. When thiobismol is given to a patient who is having a severe course of chills and fever from malaria, we do not decrease the total hours of fever in that patient but merely extend the number of hours of fever over a longer period. The value of fever per se versus some biologic factors in producing the good results of this type of therapy has not been determined. Thiobismol does not influence the temperature curve as far as the height of the fever is concerned, but it does permit of giving more fever bouts than has been the custom in the past. This is permissible because it is now possible to control the cachexia, debility and so on. This suggestion of Dr. Cole and his co-workers is valuable to those still interested in malaria.

DR. HAROLD N. COLE, Cleveland: I wish to give Dr. Schwartz of Pasadena, Calif., full credit for discovering this little trick, if you may call it that. In our work with bismuth excretion, occasionally we had to fall back on a patient with malaria as the guinea pig, as there was nobody else available in the ward. Schwartz noticed in some of these patients that following the injection there was a peculiar disturbance of the chills and he was unable to correlate it. After following a few of these he called this to my attention. It seems to be the bismuth radical that causes this for we have made experiments with the thioglycolate and find that it has no effect on it. Apparently there are other heavy metals that have an effect on malaria. The difference, however, is that you can't predict what they will do. They may stop it or it may require several injections. We have found that it has been a valuable addition to our armamentarium and that now practically all of our patients are able to have their full complement of chills where, in the past, many times it was necessary to give them quinine to save their lives.

Temper Tantrum.—If dealing with a long-continued and strongly developed behavior pattern, complete reliance upon a discourse seems to me like using a garden sprinkler to extinguish a two-alarm fire. Talking a child out of a violent temper tantrum, for example, is about as sensible as trying to allay hunger with an oration. Immobilization in blankets will calm him; spanking will only increase the excitement of an angry child.—Hohman, Leslie B., As the Twig is Bent, New York, Macmillan Company, 1940.

PROGRAM FOR INDUSTRIAL HEALTH IN STATE AND COUNTY MEDICAL SOCIETIES

CHARLES-FRANCIS LONG, M.D.
Chairman, Committee on Industrial Health, Medical Society of the State of Pennsylvania
PHILADELPHIA

Sometimes it is a pleasure not to have to begin at the beginning. In a speed-up era such as this is, I find it gratifying to be able to streamline the work of the Council on Industrial Health of the American Medical Association into one phrase, justly stating that its foundation work is so fine and familiar to all of us that we can move immediately to our problem at hand; that is, the setting up of committees on industrial health in the state societies and in the county societies.

Predicated on the good will of society presidents and boards of directors, these state committees spring easily and simply into being. And yet we know that only two thirds of our state societies have committees on industrial health, perhaps because there are still those in office among us who carry over into the present the old umbrage against the so-called "contract physician" and act as obstructionists accordingly. They do not yet appreciate that industrial health is the deep concern of every American physician and that our parent organization has gone far in comprehending this vision.

First of all, the state committee should represent all districts of the state, the general practitioner and the medical teaching faculties wherever they are present. Even more important, it should represent the medical services of large and small industries. It is a moot point whether the state department of health should be represented on the membership or whether this body should be contacted in a consulting capacity whenever needed. We feel definitely though that here is not the place for members from the specialist consulting group, for they are on the second line to be called by those who are already represented.

On its establishment, it is probable that the committee will immediately be faced with external and internal problems. The field of industrial medicine has not even been surveyed. It has lain fallow for so long that much needs be done before it can even be worked, much less be made to produce. This leads us to a plea for our newly appointed state committees on industrial health—no members who are subject to yearly appointment by changing presidential candidates can ably adopt and carry through a long-time, well planned program such as is required. It is highly important then that the committee be changed to a commission or some such more permanent form of setup, perhaps with staggered appointments so that there may be complete continuity of thought and effort.

Once the state committee form has been determined, its first efforts should be the establishment of county committees on industrial health in 100 per cent of the counties of the state. Naturally, the experience will vary from state to state in direct proportion to the number of industrial and rural counties contained within its borders. The simplest method is a letter from the chairman of the state committee to the president of

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the county society strongly urging the appointment of such a group and, if desired, giving suggestions as to ideals, aims and personnel. Gaged by the Pennsylvania experience, the industrial counties will respond promptly.

The establishment of these county committees seems doubly important. The individual physician and the individual industrial plant can be best reached by county contacts, and both need a reference group to guide and review policy. The state committee too needs the county committee as its liaison with the individual practitioner, and the county committee needs its state committee as liaison with the American Medical Association. Thus we have both a descending and ascending essential chain of communications.

TABLE 1.—*Plant Size in Pittsburgh Area*

Manufacturing establishments	1,906	Employees	189,807
Mines	50	Employees	14,682
Total	1,956		204,489
Employing 250 or more	127		6%
Employing less than 250	1,829		94%

In Pennsylvania we have set ourselves a goal which gives opportunity for a tremendous amount of work. We aim to "assure the best possible health to every worker in every industry within the state." This must be gradually approached by a coordinated program between the state and county committees and industrial organizations and labor groups. The first efforts must be a survey of the field, as we realized at our initial meeting. We proposed to do this by a questionnaire to all the physicians of the state, by data from the Department of Industrial Hygiene, and data from the chambers of commerce. Our results have been highly discouraging to date. The chambers of commerce have no data of any use to us. The Department of Industrial Hygiene has important data but it is not in a form that can be obtained without putting extra hands to work, and at present there is no money to pay the extra hands. We had hoped that at least the physicians of the state would not fail us, but they almost unanimously did. We have roughly 9,000 members in our state society. In two consecutive issues of the state medical journal we printed identical questionnaires to be returned to our committee. Of those 9,000 members, only 220 responded. But not all was completely lost. Through the question "Are you an industrial physician?" we discovered many more physicians doing industrial medicine and interested to learn more about it than any of us had suspected. This, I should say, was the only benefit we derived from the questionnaire.

However, the conviction still remains that no problem can be solved without knowing its extent. The questions which must be answered by the state committee are:

1. How many physicians are already rendering medical service to industry?
2. How many practicing physicians will devote time to learning the fundamentals of industrial health in a refresher course?
3. How many industries in the state employ 1,000 or more workers and do they have plant physicians?
4. How many industries in the state employ 250 or less workers?

Our experience would warn that the questionnaire method as we have used it is uninformative. However, this does not exhaust the possibilities or scuttle the questionnaire method. It merely proves again that personal appeal is better than eye appeal. Two suggestions for improved returns can be offered:

1. At the annual convention of the state medical society, persuade the members to answer the questionnaire as a part of their registration procedure. This has one drawback in that only 20 to 25 per cent of the total membership will attend the convention. Even at that, the figures would be better than our method has given us.

2. Send sufficient copies of the questionnaire to the secretary of each county medical society with the request that they be filled out at the next regular meeting of the society, collected at the end of the meeting and mailed back to the state committee. This, I believe, will be likely to yield the best results.

For figures on the industrial setup in each state, if your state is like mine, the state department of labor will have a census of industries showing distribution by counties and number of employed personnel, so that at least some idea can be gained as to the size of the potential demand for industrial health service. It can be taken as a good rule of thumb that industries employing 250 or less individuals have now no medical service, with the exception of those rare few who recognize that they have a peculiar industrial or toxic hazard.

The next step might be termed the sowing of the field and, as Dr. Howard Haggard put it so well recently in Philadelphia, "We must change a lot of people's folk-ways." The state committee must busy itself in assisting the practicing profession to develop adequate programs of industrial hygiene successfully in industries great and small. Let us honestly admit, right now the profession is not trained to take over such a job. We are not prepared to meet the employer's requirements or to meet the employee's expectations. The state committee should therefore be ready to submit a curriculum for refresher courses on industrial health, workmen's compensation laws and occupational disease laws to the county societies or to any other interested medical group. Whether there should be peripatetic teaching units sent throughout the state will depend on the judgment of each committee.

TABLE 2.—*Plant Size in Philadelphia Area*

Manufacturing establishments	5,537	Employees	292,691
Employing 250 or more	232		4%
Employing less than 250	5,305		96%

Further, there is a lamentable lack of familiarity with industrial health among the vast majority of our medical students. Less than 10 per cent of our seventy-seven medical schools give required undergraduate instruction in this subject, and only a few of these courses could be considered "adequate." Naturally the argument is advanced that medical school curriculums are already overcrowded and why crowd more in? We need only shift our faculty field of vision a little more toward preventive medicine than it now sees, and the curriculum time will be found. It has been allotted in the more forward looking schools, and with the help of state committees it will be provided in the rest.

Education of the employing and employed public need not require too much of our endeavors. That education is coming along rapidly enough. The various commit-

tees on industrial health of chambers of commerce and Dr. Victor Heiser's committee of the National Association of Manufacturers are seeing to it that industrial health publicity reaches into many trade journals throughout the country. You all doubtless realize that industrial health must be "hot news" if the *Saturday Evening Post* published such an excellent article as that recently written by Dr. Schramm.

The state committee will find that its work inevitably will cross many borders. It must be interested in medical ethics, in existing and new medical and workmen's compensation laws and in the fight against socialized medicine. This entails a complete rapport between itself and the other committees of the state society. But, consisting as it does of men from every corner of the whole state, it is physically impossible for the committee to have frequent joint meetings with these groups. So, unless some simpler method is devised, many joint problems remain unsolved. It is my suggestion that contact with individual committees be maintained by a single member of the committee on industrial health for each particular activity, relying on his good judgment to act for the whole committee.

As is generally true in the American scene, a fine program can succeed or fail depending entirely on local applications. Herein lies the exceeding importance of the county committees. It falls to their lot to apply the principles established by the state committee with due regard for local variation. It is up to them to smooth the relationship between industrial physicians and general practitioners. They must show the industrial physician that his field is entirely intramural, that it must be kept within the confines of the working place, stepping out only when the workmen's compensation or occupational disease laws require him to do so. These committees must show the general practitioner that the industrial physician is a case finder for him and should be treated with at least as much good grace as an old patient who brings a new one to the office.

Finally, these committees have probably the biggest job of all. It is for them to consult with employer and labor groups in providing adequate medical services to all types of workers. Paradoxically, the difficulty and need for this phase of county committee work increases as the size of the plant decreases. Let us again turn to our experience in Pennsylvania and to our two largest industrial counties, Philadelphia and Alleghany.

Philadelphia County contains 5,537 manufacturing establishments employing 292,691 individuals. But only 232, or 4 per cent, employ 250 or more employees, so that 96 per cent of all manufacturing in this county is done in plants employing from one to 250 workers. In Alleghany County the story is similar. There are 1,956 industrial firms and mines employing 204,489 persons. One hundred and twenty-seven, or 6 per cent, have 250 or more employees, or, putting the converse again, 94 per cent of all manufacturing here is done in very small plants. From these figures it is evident that 95 per cent of all industrial establishments in these counties employ less than 250 workers. Here then lie our greatest opportunities for improving industrial health. Such opportunity must be within the province of the county committees on industrial health. Their question at the moment is how to provide medical service to these small plants on an ethical basis and at a bearable cost. The answer will be furnished by demonstrations which can be successfully staged only with the active help of the county committee.

Such demonstrations have been attempted under lay auspices but not with marked success. With the help of the county society, through its committee on industrial health, demonstrations should be arranged that can forcefully and honestly depict medical service to small plants. Only by such demonstrations can the county society keep abreast of the times and assume its rightful leadership as professional director of lay interest in medical activities.

1836 Delancey Street.

HISTAMINASE IN THE TREATMENT OF ALLERGIC DERMATOSES

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The discovery by Best and McHenry [1] of an enzyme which specifically inactivates histamine suggests its use in the treatment of allergic cutaneous disorders. It has been shown that there is a release of so-called H substance in the blood during allergic shock and that this H substance may be histamine. Innumerable writers have endeavored to demonstrate the fact that histamine must be the trigger mechanism which prepares the skin for various reactions, particularly the so-called triple response of vasodilatation (streak), wheal exudative (edema) and reflex nervous dilatation (flare), which is dermatographism or urticaria itself.[2] If this fact is true, then the assumption that treatment of these allergic states with histaminase is well founded and worthy of an extended trial before being discarded as another false hope in the long list of attempts to combat the allergic dermatoses.

Histamine may be obtained from the liver, lungs, skin and other body tissues in a pure form under aseptic conditions.[3] It is preformed in the cell in a slightly inactive form and is readily released into the surrounding area. This release is not entirely dependent on the destruction of the cells but may occur when the cells receive stimulation of a certain intensity, and the magnitude of this stimulation is dependent on the allergic irritability of the individual cells. The fact that very little histamine is found in the urine after the intravenous injection of large amounts of the substance [4] led Best and McHenry to study distribution, properties and action of the substance or system producing this inactivation.

Histamine inactivating material was first demonstrated in horse lung and subsequently in beef lung, liver and kidney. The kidneys, duodenum, jejunum and cecum each inactivated the greatest amount of histamine, and the kidney was more active than any other tissue in inactivating histamine.

Histaminase is a compound of physiologic albuminoid substance obtained from the intestinal mucous membrane. It is a loose white powder which is stable and

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The histaminase was supplied by M. A. Hilger of the department of medical research of the Winthrop Chemical Company, Inc., which markets this product under the proprietary name Torantil (T 360).

1. Best, C. H., and McHenry, E. W.: The Inactivation of Histamine, J. Physiol. **70**: 349 (Dec.) 1930.

2. Stokes, J. H.; Kulchar, G. V., and Pillsbury, D. M.: Effect on the Skin of Emotional and Nervous States, Arch. Dermat. & Syph. **31**: 470 (April) 1935.

3. Best, C. H.; Dale, H. H.; Dudley, H. W., and Thorpe, W. V.: The Nature of the Vasodilator Constituents of Certain Tissue Extracts, J. Physiol. **62**: 397 (March) 1927.

4. Oehme, C.: Arch. f. exper. Path. u. Pharmakol. **72**: 76, 1913.

dissolves in water to a slightly opalescent fluid. This preparation is put up as a dry powder of 2 histamine detoxicating units and in tablets enterically coated of 5 units. The unit is the amount necessary to inactivate 1 mg. of histamine during twenty-four hours' incubation at 37 C. in a phosphate buffer solution at a p_H of 7. Chemically histaminase is diamineoxydase.[5] The change produced in histamine during inactivation appears to be oxidative since it is inhibited by potassium cyanide, and under anaerobic conditions it is accelerated by oxygen. It is suggested that rupture of the iminazole nucleus occurs in the histamine or that a complex nondialyzable compound is produced. Reduction of the iminazole value parallels the degree of inactivation of histamine.

Roth and Horton[6] determined the normal response of gastric acidity to subcutaneous injection of histamine. Several days after the response had been accurately established, histaminase was introduced into the duodenum from twenty-five to thirty minutes before the subcutaneous injection of histamine. This practically abolished the rise of gastric acidity. Likewise subjects were immersed in water at 24 C., and the curve of their gastric acidity under such conditions was similar to that caused by histamine. As before, the introduction of histaminase abolished the rise in gastric acidity. In similar fashion, when histaminase was injected intramuscularly thirty minutes before the usual subcutaneous injections of histamine, the rise in gastric acidity was abolished. This is physiologic evidence that histaminase administered to man will inhibit the action of histamine and contrary to the work of Atkinson and Ivy,[7] although they injected their histaminase intravenously instead of introducing it directly into the duodenum.

Karady and Browne[8] carried out experiments to determine what effect pretreatment with histaminase might have on histamine and anaphylactic shock in animals. They used thirty guinea pigs. The jugular vein of twenty pigs was exposed under slight ether narcosis and 3 units of histaminase dissolved in 2 cc. of physiologic solution of sodium chloride was injected. In fifteen minutes all thirty received 4 mg. of histamine dihydrochloride intra-abdominally. In from five to seven minutes all the nontreated animals were in histamine shock; seven died. Two of the pretreated animals died in thirty-five minutes; all the rest survived. Thirty guinea pigs were sensitized with 3 cc. of 50 per cent egg white subcutaneously. From two to three weeks later twenty guinea pigs were injected with histaminase under the same conditions as previously described. After fifteen minutes all received 2 cc. of 50 per cent egg white intra-abdominally. Four of ten animals of the control group died in from ten to fourteen minutes; all had symptoms of anaphylactic shock in four or five minutes. None of the pretreated group died.

Horton and Roth[9] described a case of hypersensitivity to cold, which case they had followed since 1927. They concluded that urticaria produced by hypersensitivity to cold was due to an overabundance of histamine. They treated their patient with subcutaneous injections of 0.1 mg. of histamine dihydrochloride weekly in an effort to increase the patient's tolerance to histamine. The patient improved. Later they[10] treated a similar case with histaminase, administering 67 units in four and one-half days. He too improved.

Gilbert and Goldman[11] prepared bronchioles for microscopic examination. The size of the bronchiole was recorded by the use of a camera lucida. The addition of 3 mg. of histamine acid phosphate usually resulted in complete closure of the bronchiolar lumen. The preparation was observed for about ten minutes in order to rule out spontaneous relaxation and then the test drug was added. Histaminase caused slight dilatation of histamine-poisoned bronchioles in three experiments and no effect in two. After twenty-four hours' incubation at 37 C. a mixture of histaminase and histamine caused marked contraction of normal bronchioles in four experiments. Their conclusions were that histaminase is unable to prevent the action of histamine on these preparations.

Foshay and Hagebusch[12] believe that serum sickness with its urticarial manifestations is due to release of histamine in the tissues and circulation consequent on the union of serum protein antigens and antibodies. Six of eight patients with serum sickness received complete relief from 5 units of histaminase given orally three times daily. Within thirty-six hours all these patients had relief from their intolerable pruritus, patchy erythema and urticaria. Twelve patients were treated twice daily with the injectable form. Within seventy-two hours none of the patients had any further symptoms. They expressed optimism for the prophylactic use of histaminase in the prevention of serum sickness and further stated that this method of treatment is the only rational, genuinely effective and safe remedy known for this distressing condition. Moldenschardt[13] treated five patients who had cutaneous disorders with histaminase, two of whom had eczema, one Quincke's edema, one a moist erythema associated with marked pruritus and one serum sickness following diphtheria antitoxin injections. All responded and recovered within a short time. Adelsberger[14] reported excellent results with histaminase treatment in three cases of allergic eczema on a nutritional basis and one case of light dermatitis. Hartmann[15] stated that twenty-five patients with severe acne conglobata who had failed to respond to all types of medical treatment showed remarkable improvement after four or five injections of histaminase. In most of the twenty-five cases there existed some digestive disorder. Blecha[16] treated twelve children who had allergic eczema with oral and intramuscular histaminase; five were completely cured, three greatly improved and the remainder were unaffected. Laymon and Cumming[17] treated seventeen

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8. Karady, S., and Browne, J. S. L.: Effect of Histaminase Treatment on Histamine and Anaphylactic Shock in Guinea Pigs, J. Immunol. **37**: 463 (Nov.) 1939.

9. Horton, B. T., and Roth, Grace M.: Proc. Staff Meet., Mayo Clin. **12**: 7 (Jan. 6) 1937.

10. Roth, Grace M., and Horton, B. T.: Proc. Staff Meet., Mayo Clin. **12**: 129 (March 3) 1937.

11. Gilbert, A. J., and Goldman, F.: The Effect of Aminophyllin, Histaminase and Nicotinic Acid on Histamine-Poisoned Puppy Bronchioles, Bull. John Sealy Hospital and School of Medicine, University of Texas **2**: 55 (March) 1940.

12. Foshay, Lee, and Hagebusch, O. E.: Histaminase in the Treatment of Serum Sickness, J. A. M. A. **112**: 2398 (June 10) 1939.

13. Moldenschardt, H.: Torantil, ein aus Darmschleimhaut gewonnenes Präparat, Med. Klin. **32**: 153 (Jan. 31) 1936.

14. Adelsberger, L.: Fortschr. d. Therap. **13**: 568 (Oct.) 1937.

15. Hartmann, M.: Ueber die Behandlung der Akne vulgaris mit Torantil, Dermat. Wchnschr. **106**: 693 (June 18) 1938.

16. Blecha: Med. Klin. **34**, Feb. 11, 1938.

17. Laymon, C. W., and Cumming, H. A.: Histaminase in the Treatment of Urticaria and Atopic Dermatitis, J. Invest. Dermat. **2**: 301-308 (Dec.) 1939.

patients who had urticaria with histaminase and recorded the following results: 59 per cent cured, 12 per cent improved and 29 per cent unimproved; no definite improvement in eight cases of atopic dermatitis, and it was of no value in two cases of dermographism. Forman [18] stated that this therapeutic agent offers a new and helpful approach to the treatment of urticaria, angioneurotic edema and atopic dermatitis. In his report of thirteen cases of urticaria, all but one showed improvement, two of three cases of atopic dermatitis showed improvement, two of four cases of contact dermatitis showed improvement and one case of pruritus was controlled by histaminase. Urbach [19] reported the successful treatment with histaminase of a woman aged 31 with severe purpura; vitamin C had been tried without any beneficial results. He concluded that in this instance the purpura was due to a deficient detoxifying function of the intestine. Matras, in discussing this case, mentioned one of chronic urticaria which had not been benefited by injections of histaminase. Baker [20]

Treatment with Histaminase

Diagnosis	No. of Cases	Results	Comment
Twenty-Five Cases Under Oral Treatment			
Papular urticaria	1	Clinically cured	Histaminase used alone
Atopic dermatitis	3	Improved	Histaminase in conjunction with other therapy
Dermographism	2	Unimproved	Histaminase used alone
Allergic eczema	3	2 unimproved 1 improved	Histaminase in conjunction with other therapy
Chronic urticaria	13	8 clinically cured 5 unimproved	Histaminase used alone
Idiopathic pruritus	3	Slight improvement	Histaminase used alone
Ten Cases Under Injection Treatment			
Chronic urticaria	10	All improved	Fever up to 102 F. after first injection, general malaise, pain at site of injection; mild rises in temperature after second and third injections, very little thereafter

reported two cases of cold urticaria which responded to treatment with histaminase. The first patient had a severe generalized headache, palpitation and general tremulousness associated with the urticaria. These symptoms subsided with the onset of the localized edema. Histaminase tablets were used simultaneously with gradual desensitization to cold. The results of the treatment were most gratifying. The second patient was treated similarly with the same good results. Kile and Rusk [21] treated a patient who had cold urticaria with histaminase without any results. They did not mention the amount used or the length of time it was tried. Miller and Piness [22] treated forty-two patients with histaminase; twenty-nine had urticaria, and only five were relieved; five had allergic dermatitis, and none were relieved. They felt that in no instance could this relief be unequivocably attributed to the use of the enzyme. They reported few untoward reactions.

The histamine-histaminase reaction is an oxidative one, and as yet I have observed no untoward reactions. There is no need to worry about the type of reactions that occur when a patient is treated with small doses of histamine such as flushing of the face, shivering or faintness, fall in blood pressure, rise in pulse rate, headache, anginal pains in the chest or shock.

My purpose in this paper is to picture the results of treatment of various allergic cutaneous disorders with histaminase, orally and by injection, and to demonstrate that it might be a valuable adjunct in the management of these cases. All the cases studied were taken from private practice and analyzed from the clinical point of view. In some of them histaminase was used by itself while in others it was a part of the advised therapy. When it was not the only therapeutic agent, the patients had been rebellious to other routine treatment measures. Twenty-five patients received histaminase by mouth; these may be subdivided as follows: thirteen had recurrent urticaria, three had allergic eczema, one had papular urticaria and three had pruritus. Ten patients with recurrent urticaria received intramuscular injections of histaminase 2 cc. every other day for a minimum of six injections and a maximum of twelve. The initial reactions of fever, malaise and joint pains following intramuscular injections of histaminase in 2 cc. doses suggests the possibility of a foreign protein reaction. However, the same type of reaction does not always occur after the second or third injection, which does not hold true for reactions following injections of whole milk and other nonspecific proteins. This requires further investigation of the injectable material. All the patients so treated showed marked improvement, and after treatment was discontinued no recurrences have been noted up to the present time.

SUMMARY

This group of thirty-five cases is too small a series to permit any dogmatic statements. In several cases the use of histaminase alleviated all the symptoms while in others it was a very useful factor in controlling the pruritus. Histaminase is no more a cure-all for allergic cutaneous conditions than are allergens the sole major excitants in the same diseases. Furthermore, it must be remembered that histaminase is a protein preparation and probably contains a variety of proteins which might cause reactions in patients whose allergy is of a protein type. It is possible that treatment with histaminase may give the epidermal structures relief from histamine excitation and help it build tolerance to histamine in the same way that intravenous injections with histamine in the treatment of chronic urticaria produces a gradual unresponsiveness of the skin to "H substance," which is thought to be responsible for whealing, as believed by Alexander.[23] I know that there has been no established fact that histamine is the causative agent in any pathologic condition and that most of the present data may be presumptive. Nevertheless evidence has been presented showing that histaminase oxidizes histamine in the body and on this basis its therapeutic assistance in the treatment of allergic dermatoses may be justifiable.

18. Forman, Jonathan: The Use of Histaminase in the Treatment of Various Allergic Manifestations, Ohio State M. J. **36**: 56 (Jan.) 1940.
19. Urbach, E.: Intestinal-toxisch bedingter Character einer chronisch rezidivierenden Purpura durch Torantil Festgestellt, Zentralbl. f. Haut. u. Geschlechtskr. **54**: 70, 1936.
20. Baker, T. W.: Histaminase in the Treatment of Cold Allergy, J. A. M. A. **114**: 1059 (March 23) 1940.
21. Kile, R. L., and Rusk, H. A.: A Case of Cold Urticaria with an Unusual Family History, J. A. M. A. **114**: 1067 (March) 1940.
22. Miller, Hyman, and Piness, George: Histaminase in the Treatment of Allergy, J. A. M. A. **114**: 1742 (May 4) 1940.
23. Alexander, H. L., and Elliot, R.: Treatment of Chronic Urticaria with Intravenous Injections of Histamine, read before the Central Society for Clinical Investigation in October 1939.

CONCLUSION

Histaminase oxidizes histamine in the body and is a helpful factor in the treatment of allergic dermatoses. A small group of thirty-five patients with various allergic dermatoses was treated with histaminase, orally and by injection. There was partial or total improvement noted in all but nine of the patients treated. I can draw no definite conclusions regarding the dosage of histaminase, since each case must be studied individually. However, as yet no untoward reactions have been noted after patients have taken as much as 150 histamine detoxicating units daily for four or five days. Patients receiving intramuscular injections of histaminase had very much better results than those receiving the enzyme in tablet form. The first four injections elicited symptoms comparable to those following foreign protein shock therapy. Further clinical and laboratory data are necessary before any definite conclusions can be drawn regarding the specific value of histaminase.

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ABSTRACT OF DISCUSSION

Dr. G. Marshall Crawford, Boston: Dr. Goldberg has reviewed the rationale of histaminase. Its physiology, chemistry and mode of action were discussed, but this is mostly presumed knowledge. It is also based on what is known or presumed about histamine and assumed that histamine is the so-called H substance. Failure of this presumably ideal treatment should lead us to doubt whether histamine is actually that H substance. At least it may not be the only H substance, or some other agent may play a part in certain cases. It seems to act as a trigger mechanism part of the time. If histaminase will break a link in the chain of the allergic reaction, that may be its most valuable function. This might increase the magnitude of stimulus necessary to initiate allergic reaction, in other words decrease the allergenic irritability of tissues. If so, this could allow us to work backward in determining the cause of allergy. Whether histaminase interrupts an antigen-antibody reaction or brings about oxidation or deamination could then perhaps be determined. Possible foreign protein action, as mentioned by Dr. Goldberg, should be considered carefully, especially with the intramuscular injection. A review of the literature shows that about a dozen conditions have been treated with histaminase. Best results were obtained in serum sickness, physical allergy, angioneurotic edema and some chronic urticaria. In other diseases, results are questionable. At the Massachusetts General Hospital we have studied about twenty-five cases, with the following results: Treatment of three actinic and one cold allergy cases gave fairly satisfactory results. The cold urticaria was completely relieved as long as the treatment was continued. Two cases of actinic urticarias were 80 per cent relieved and one eczema solare was untouched. Fifteen cases of chronic urticaria of from three months' to fifteen years' duration were unsatisfactory. In two the condition was somewhat worse, possibly because of pork sensitivity. Histaminase is obtained from the hog. We gave orally up to 300 units daily. Six cases of dermographism were entirely unresponsive. Our resident, Dr. Capland, has followed these more closely and is more pessimistic than our results indicate. In physical allergy, however, there is a fair degree of success. Dr. Goldberg's emphasis on the presumption of the mode of action of this drug is well justified. I agree that histaminase is no cure-all, and I should like to reemphasize again the possibility of foreign protein action. The plea for further trial before discarding this agent is worth while.

Dr. Ashton L. Welsh, Cincinnati: I happen to have had the opportunity to use histaminase in a group of six cases of lichen urticatus. All six cleared completely on histaminase in large doses. Three were followed for more than one year and have remained clear. The other three were lost after from one to two months' observation. I have also had one patient with cold urticaria which has completely cleared and remained clear. Other patients with other forms of urticaria and with atopic eczema did not show such a favorable response and have not been controlled well enough or followed long enough to admit of critical appraisal.

Dr. Herman Goodman, New York: Success or failure of a drug such as histaminase depends on what one prescribes it for and when it is given. For many years it has been recognized that, no matter what the irritant, the effect on the skin has been very much the same. There are limited modes of reaction by the skin to numerous unrelated injuries or insults. In the discussion of histaminase in the treatment of allergic dermatoses, it is contended that the effect of histaminase is not on the irritant histamine in the sense that it has been mentioned this morning. The irritant effect is on preventing the formation of the histamine. Histidine is the precursor of histamine. Histamine is formed on injury to protein of which histidine is a component. Histidine is five times as prevalent in skin protein as any other tissue. To be effective, histaminase must prevent the decarboxilation of histidine. Therefore, to prevent the action of histidine it is necessary to have an agent, which histaminase is held to be, which will break the chain between histidine and histamine. The same agent fails if given long after histamine has done its damage. The greatest success of histaminase is in cold allergy, which is the response to insult to the continued presence of histamine resulting from decarboxilation of histidine. One does make it possible for the person to expose himself to cold without giving evidence of his cold allergy by reason of the fact that by the administration of histaminase the decarboxilation of histidine has been interrupted. Results are to be expected of histaminase if one recalls histidine, its decarboxilation, and the formation of histamine which is the activating cause of the response of the skin.

Dr. Herman Sharlit, New York: I want to endorse what Dr. Goodman just said. Histaminase cannot cure the condition which it alleviates. Histaminase succeeds, where it does succeed, only in placing a block in the machinery of the production of a sign, if given at a proper moment, and when removed has no influence on successive episodes in the production of the symptom. In other words, if we are dealing with a successful treatment of urticaria by histaminase, if on the cessation of the use of histaminase we get no further urticaria, the cure has not heen achieved by the histaminase; whatever the cure, that remains a mystery; but histaminase has given the interim, has given the time to suppress symptoms to a time when they were no longer spontaneously produced. A patient had urticaria limited to the face for two years daily without interruption, in spite of every approach from the point of view of external irritants or ingested foods. Everything conceivable had been tried to stop this urticaria. When I first saw this victim, she was beginning to develop, in addition to hives, edemas of the lip and the eye. I gave her fifteen tablets of histaminase at once. The next day she had no urticaria for the first time in two years. She continued histaminase fifteen tablets a day for three days without any recurrence of the urticaria. On the fourth day I advised the reduction to two tablets three times a day and the urticaria returned. The situation is now exactly that, three months afterward: namely, so long as she takes fifteen tablets of histaminase a day, she has no urticaria; when she reduces it or gives it up for one day, the urticaria is back again. Until she either spontaneously breaks the causative link or it is discovered and destroyed, she will persist in having urticaria. But from the point of view of clinical results, I continue to relieve her by the persistent use of histaminase.

Dr. Lawrence C. Goldberg, Cincinnati: I do not feel that histaminase is a cure-all for any of the allergic conditions. As I tried to emphasize, it may be a helpful adjunct but we know that allergic conditions are variable and change from time to time. There are many factors that have to be thought of. I think that Dr. Goodman to some extent misconstrued my feeling about this drug, because I still would like to emphasize that it does not cure allergic conditions as we find it at the present moment. But it may help, and, if so, I think it should be tried. The drug should be kept in an ice box where it can always be cold. Large doses should be given, one or two tablets every hour, so that the level is consistent with the amount of histamine-like substance which may be set off in the body.

VERTEBRAL FRACTURES AS A COMPLICATION OF CONVULSIONS

IN HYPOGLYCEMIC SHOCK AND METRAZOL THERAPY IN PSYCHIATRIC DISORDERS

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In a previous communication we presented the frequent complication of vertebral fractures in the course of metrazol therapy in psychiatric disorders.[1] At that time, in a roentgenographic study of fifty-one psychiatric patients who had received treatment with metrazol, twenty-two (43.1 per cent) manifested compression fractures of the vertebrae, most commonly in the midthoracic region, and in most instances the fractures of the vertebral bodies were multiple. Fragmentation and compression of the anterior portion of the upper surface of the body occurred frequently, while in about half the cases the fractures manifested themselves only by a slight forward displacement of a disklike fragment of the upper portion of the body. There was a higher incidence of fractures in female (sixteen) than in male (six) patients.

At the time of the first report it was indicated that a study was being made of the effect of keeping the patient on his side in an acutely flexed position, since it was felt that the force of sudden flexions of the spine, which may be the cause of the vertebral fractures, would thereby be reduced.

The present report is an extension of our previous studies and includes a roentgenographic survey of the following groups: (1) patients who manifested convulsions during the course of hypoglycemic shock therapy; (2) patients who had received both hypoglycemic shock and metrazol therapy, with convulsions occurring during the insulin shock; (3) patients who were placed in the position of acute flexion during the treatment with metrazol; (4) a control series of patients who received hypoglycemic shock therapy but who had no convulsions, and also an untreated group of patients whose spines were examined roentgenographically.

Sakel [2] describes two types of hypoglycemic shock: the "wet shock," during which the patient sweats profusely, grows somnolent and goes into deep coma, and the "dry shock," during which an epileptic attack occurs in the second or third hour of hypoglycemia. He states that the type of response cannot be predicted in advance and is independent of the size of the dose. Early in the work on hypoglycemic shock therapy there was a difference of opinion as to the therapeutic value of these convulsions. At first, when they occurred, the shock was immediately interrupted by intravenous dextrose. Later, Sakel [3] clarified this point by stating that in the "dry shock" the epileptic seizure is not dangerous and one may wait a few minutes before terminating the hypoglycemia by nasal tube. However, if the epileptic seizure occurs in the fourth or fifth hour of hypoglycemia there is presented a very dangerous situation, and hypoglycemia must be terminated at once by intravenous dextrose. Recently Sakel [4] has specified that metrazol may be used to produce convulsions during the hypoglycemia in certain types of resistant cases and emphasizes that the therapeutic value of epileptic seizures was recognized in certain cases from the beginning of the insulin shock treatment.

Plattner and Frölicher, as quoted by Thomas and Wilson,[5] state that in their series of cases convulsions occurred in 7.7 per cent of comas of unresponsive cases but in only 3.2 per cent of comas of remitting cases. Young and his co-workers [6] encountered convulsions in 16 per cent of patients treated with insulin. Malzberg [7] in a statistical study of 1,039 insulin-treated patients from the various New York state hospitals, found that 394 patients (38 per cent) had convulsions ranging in number from one to eleven and over. Of these, 220 (55 per cent) were males and 174 (44 per cent) were females. A survey of the literature reveals no report of the occurrence of vertebral fractures in the course of hypoglycemic shock therapy. Recently it was called to our attention that Stalker [8] reported a case of vertebral compression fracture due to convulsions induced by triazol, the chemical composition of which resembles that of metrazol.

TABLE 1.—*Vertebral Fractures in Patients Treated with Shock Therapy*

Classification of Patients	Number of Patients		
	Male	Female	Total
Patients treated with insulin shock	89	84	173
Patients with insulin convulsions	40	22	62
(*a*) Early convulsions, 33	(65%)	(35%)	(36%)
(*b*) Late convulsions, 195			
Patients with convulsions treated with insulin alone	31	15	46
(*a*) Patients examined roentgenographically	22	12	34
(*b*) Patients with vertebral fractures	6	1	7 (20.5%)
Patients treated with both insulin and metrazol	9	7	16
(*a*) Patients examined roentgenographically	6	6	12
(*b*) Patients with vertebral fractures	1	2	3
Patients treated with metrazol in position of acute flexion	1	6	7
(*a*) Patients examined roentgenographically	1	6	7
(*b*) Patients roentgenographed prior to treatment	1	3	4
(*c*) Patients with vertebral fractures	1	4	5

Up to the present time 173 patients have been treated at the Psychiatric Institute with hypoglycemic shock therapy, the greatest number of whom were schizophrenic. Of these, eighty-four were females and eighty-nine males. Convulsions varying from one to twenty in number occurred in sixty-two patients (36 per cent), of whom twenty-two (35 per cent) were females and forty (65 per cent) were males (table 2). The total number of convulsions in the series of insulin-treated patients was 228 and the average number was 3.6. Considering those convulsions which occur in the second and

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3. Sakel, Manfred, in Discussion on Hypoglycemia Symposium, Am. J. Psychiat. **94**: 181-182 (July) 1937.

4. Sakel, Manfred: The Pharmacological Shock Treatment of Schizophrenia, authorized translation by Joseph Wortis, Nervous and Mental Disease Monograph 62, New York, Nervous and Mental Disease Publishing Company, 1938.

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6. Young, G. A.; Young, R. H., and Rouck, Louis: Experiences with the Hypoglycemic Shock Treatment of Schizophrenia, Am. J. Psychiat. **94**: 159-170 (July) 1937.

7. Malzberg, Benjamin: Outcome of Insulin Treatment of One Thousand Patients with Dementia Praecox, Psychiat. Quart. **12**: 528-553 (July) 1938.

8. Stalker, Harry: Double Vertebral Compression Fracture from Convulsion Therapy, Lancet **2**: 1172-1173 (Nov. 19) 1938.

third hour of hypoglycemia as "early" and those occurring in the fourth and fifth hour as "late," there were thirty-three of the former type and 195 of the latter. Of the sixty-two insulin-treated patients manifesting convulsions during hypoglycemia, sixteen subsequently had a course of metrazol therapy. Consequently only forty-six patients, fifteen females and thirty-one males, had convulsions during hypoglycemia without any other complicating therapy. Of these, thirty-four were available for roentgenographic study, twenty-two males and twelve females. Compression fractures of the vertebrae were observed in seven (20.5 per cent) patients, six males and one female. In six of these patients late convulsions had occurred.

Of the sixteen patients (nine males and seven females) who had both insulin and metrazol treatment, roentgenograms were obtained for twelve, six males and six females. Compression fractures of the vertebrae were found in three of these cases. In this group there were one male and two females.

With the hope of preventing compression fractures of the vertebrae in the course of metrazol therapy, we have treated seven patients, six females and one male, in the position of acute flexion. Roentgenograms showing no abnormalities of the spine were obtained for four of these patients prior to treatment. After several metrazol-induced convulsions, five patients, four females and one male, showed compression fractures of the vertebrae (table 1).

It is noteworthy that two of these patients had previously had convulsions during a course of hypoglycemic shock and showed no fractures on roentgenographic

TABLE 2.—*Detailed Study of Patients Manifesting Convulsions and Vertebral Fractures in Hypoglycemic Shock and Metrazol Therapy*

Case No.	Name	Age	Diagnosis	Number of Insulin Convulsions	Number of Metrazol Convulsions	X-Ray Report *
Female Patients						
1	F. S.	18	Schizophrenia, catatonic	6	Not treated †	Negative
2	R. K.	24	Schizophrenia, hebephrenic	2	Not treated	Negative
3	N. S.	27	Schizophrenia, hebephrenic	3	10	Negative
4	S. C.	19	Schizophrenia, catatonic	3	Not treated	Not available
5	G. Z.	26	Schizophrenia, catatonic	1	Not treated	Negative
6	M. Z.	24	Schizophrenia, hebephrenic	5	Not treated	Negative
7	C. J.	16	Schizophrenia, hebephrenic	2	Not treated	Not available
8	A. P.	48	Schizophrenia, paranoid	1	Not treated	Not available
9	F. M.	16	Psychoneurosis, obsessive compulsive	8	Not treated	Negative
10	T. K.	23	Schizophrenia, hebephrenic	11	Not treated	Negative
11	A. C.	22	Schizophrenia, paranoid	4	Not treated	T 4-5
12	S. M.	22	Schizophrenia, catatonic	2	Not treated	Negative
13	S. H.	35	Schizophrenia, catatonic	1	3	Negative after insulin; fracture T 5-6-7-8 after metrazol
14	A. K.	31	Schizophrenia, hebephrenic	3	Not treated	Negative
15	K. F.	29	Schizophrenia, catatonic	1	Not treated	Negative
16	F. J.	33	Schizophrenia, paranoid	1	5	Negative after insulin; negative after metrazol in position of hyperextension
17	B. K.	22	Schizophrenia, hebephrenic	8	22; combined insulin and metrazol 12	Negative
18	B. H.	30	Schizophrenia, paranoid	20	14	Not available
19	G. C.	17	Schizophrenia, catatonic	5	19	T 6-7-8
20	L. C.	25	Schizophrenia, mixed	5	3	T 7-8
21	M. G.	17	Schizophrenia, hebephrenic	2	5	Negative
22	S. B.	30	Manic-depressive, agitated depression	1	3	Negative
Male Patients						
23	N. M.	18	Schizophrenia, catatonic	3	18	T 4-5
24	G. S.	14	Schizophrenia, hebephrenic	2	15	Negative
25	L. S.	15	Schizophrenia, hebephrenic	5	Not treated	T 6-8
26	B. W.	17	Schizophrenia, catatonic	3	1	Negative
27	J. P.	15	Schizophrenia, hebephrenic	7	13	Not available
28	S. M.	23	Schizophrenia, catatonic	5	14	Negative
29	J. G.	26	Schizophrenia, hebephrenic	1	Not treated	Not available
30	J. F.	31	Schizophrenia, paranoid	1	Not treated	Negative
31	S. W.	15	Schizophrenia, hebephrenic	2	7	Negative
32	S. G.	34	Schizophrenia, paranoid	1	Not treated	Negative
33	J. Q.	46	Schizophrenia, paranoid	2	Not treated	Not available
34	L. G.	15	Schizophrenia, simple	3	Not treated	Negative
35	T. O.	22	Schizophrenia, hebephrenic	4	Not treated	T 5
36	A. M.	16	Schizophrenia, hebephrenic	2	Not treated	Not available
37	I. H.	33	Schizophrenia, hebephrenic	2	Not treated	Negative
38	L. B.	18	Schizophrenia, hebephrenic	6	Not treated	Not available
39	M. H.	18	Schizophrenia, hebephrenic	4	Not treated	T 4-5
40	J. M.	20	Schizophrenia, catatonic	7	22	Not available
41	J. C.	13	Schizophrenia, catatonic	3	9	Negative after insulin; fracture T 9-10-11 after metrazol
42	R. M.	21	No psychosis, epileptic personality	1	Not treated	Not available
43	D. G.	22	Schizophrenia, simple	1	Not treated	Not available
44	R. H.	20	Schizophrenia, hebephrenic	8	Not treated	Negative
45	M. S.	18	Schizophrenia, simple	2	Not treated	Negative
46	J. M.	23	Schizophrenia, hebephrenic	2	Not treated	Not available
47	C. S.	21	Schizophrenia, hebephrenic	3	Not treated	T 7
48	E. P.	19	Schizophrenia, hebephrenic	2	Not treated	Negative
49	M. M.	19	Schizophrenia, hebephrenic	5	Not treated	Negative
50	F. W.	33	Schizophrenia, hebephrenic	2	Not treated	T 6-7
51	L. H.	17	Schizophrenia, mixed	4	Not treated	Negative
52	T. S.	27	Manic-depressive, depressed	4	Not treated	T 6-7
53	M. D.	25	Schizophrenia, paranoid	1	Not treated	Not available
54	C. L.	27	Psychosis with chronic encephalitis	5	Not treated	Negative
55	H. J.	30	Schizophrenia, hebephrenic	1	16	Negative
56	J. F.	20	Schizophrenia, hebephrenic	2	Not treated	Negative
57	L. C.	18	Schizophrenia, catatonic	2	Not treated	Negative
58	H. B.	11	Schizophrenia, hebephrenic	5	Not treated	Negative
59	D. T.	5	Psychosis with mental deficiency	6	6	Not available
60	J. P.	8	Schizophrenia, hebephrenic	4	Not treated	Negative
61	M. M.	5	Psychosis with mental deficiency	8	Not treated	Negative
62	A. H.	3	Schizophrenia, undetermined	2	Not treated	Not available

* The letter T and the number represent a compression fracture of the corresponding thoracic vertebra. † Not treated with metrazol.

examination, whereas, after a few metrazol-induced convulsions were given compression fractures of the thoracic vertebrae were demonstrated.

As a control series we have used a group of twenty-eight patients, seven males and twenty-one females, who had roentgenograms of the thoracic spine. Twenty of these patients have received or are receiving insulin shock treatment, but in none of them have there been frank epileptoid convulsions, although ten have had tonic spasms, rigidity of the arms, severe twitchings, marked myoclonic movements and generalized tremors. Eight patients are newly admitted and have had routine roentgenograms of the spine. In none of these twenty-eight patients was there any evidence of injury to the thoracic vertebral bodies.

In treating patients with metrazol, we are now utilizing a position of hyperextension. The patient, lying supine, has an air cushion placed along the thoracolumbar region of the back. The metrazol injection is then given, and during the convulsion the spine is limited in activity as much as possible by nurses holding the shoulders and pelvis, but not too rigidly. Our experience has been too limited to pass any judgment as to the efficacy of this method.

It is probable that the fractures of the mid-dorsal vertebrae are due to sudden acute flexion of the spine. Since the extensor group of muscles of the spine are weakest in the mid-dorsal region, the vertebral column secures the least amount of protection against flexion in this area.

The fractures seen following insulin convulsions were similar in nature to those sustained following the use of metrazol. They were, however, less extensive, and as a rule fewer vertebrae were involved.

Fig. 1 (case 52).—A white man aged 27 with a manic-depressive psychosis of the depressed type had four convulsions during the course of hypoglycemic shock therapy. A roentgenogram then revealed compression fractures of the sixth and seventh thoracic vertebrae.

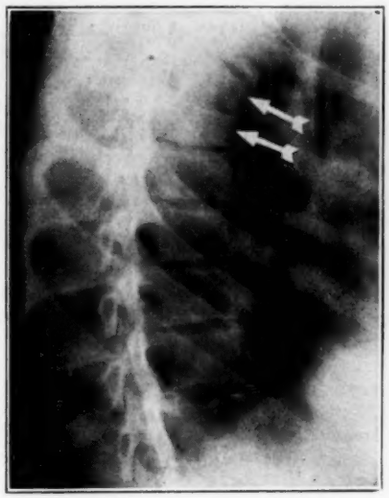

Fig. 2 (case 39).—A white youth aged 18 with schizophrenia had four convulsions during the course of hypoglycemic shock therapy. A roentgenogram then revealed compression fractures of the fourth and fifth thoracic vertebrae.

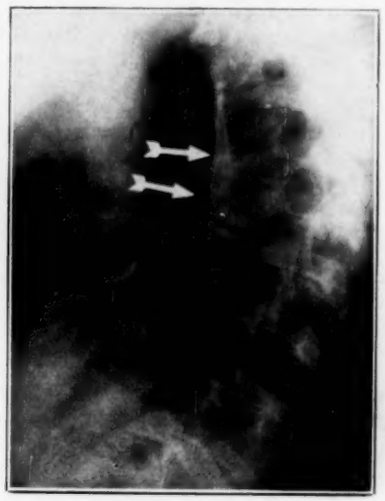

Fig. 3 (case 23).—A youth of 18 with schizophrenia had four convulsions during hypoglycemic and eighteen during metrazol therapy. Compression fractures of the fourth and fifth thoracic vertebrae, with evidence of bone production over the anterior margins of both vertebrae, were revealed.

REPORT OF CASES

CASE 52.—T. S., a white man aged 27, married, was admitted to the Psychiatric Institute April 19, 1937, with a diagnosis of manic-depressive psychosis, depressed type, of nine months' duration. The patient was well nourished, of pyknic habitus, and showed no pathologic condition on physical or laboratory examination. Hypoglycemic shock therapy was instituted September 28. On the fifteenth day of treatment with a dose of 125 units of insulin, the patient reached coma at 11:30 a. m. and had an epileptoid convulsive seizure fifteen minutes later. On the thirty-second treatment day, with a dose of 110 units, his second convulsion developed at 11:10 a. m. A third convulsion occurred on the thirty-eighth day with a dose of 90 units, at noon. The fourth and last convulsion occurred at 11 a. m. on the forty-fifth day, with a dose of 80 units. In all, he had thirty-three comas, and hypoglycemic shock therapy was terminated December 6, the patient being much improved. He was discharged as recovered March 1, 1938.

Approximately a year later, March 27, 1939, the patient was recalled for investigation, at which time stereoscopic roentgenograms revealed compression fractures of the sixth and seventh dorsal vertebrae. He had not at any time complained of back pain (fig. 1).

CASE 39.—M. H., a white youth aged 18, single, was admitted to the Psychiatric Institute March 14, 1938, with a diagnosis of dementia praecox, hebephrenic type, of one and one-half years' duration. He was well nourished, of asthenic habitus, and presented no pathologic changes on physical or laboratory study. He was placed on hypoglycemic shock therapy May 31. On the twenty-second treatment day, with a dose of 150 units of insulin, the patient had an epileptoid convulsive seizure at 9:25 a. m. On the twenty-eighth treatment day, with a dose

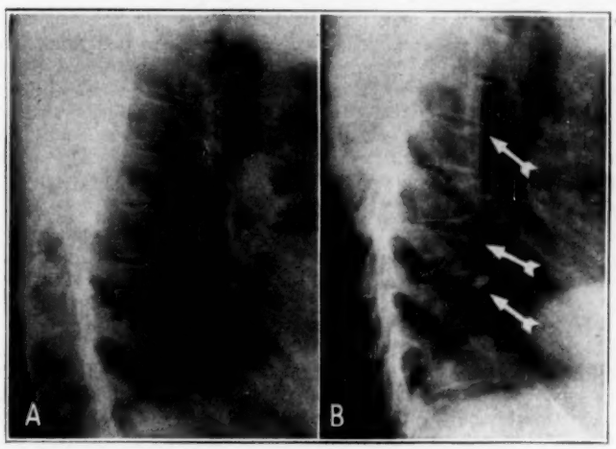

Fig. 4 (case 13).—A white woman aged 33 with schizophrenia had one convulsion during a course of hypoglycemic shock therapy. A roentgenogram (*A*) then revealed no abnormalities of the thoracic vertebrae. After three metrazol-induced convulsions a roentgenogram (*B*) revealed compression fractures of the fifth, sixth, seventh and eighth thoracic vertebrae. The patient had been placed in the position of acute flexion during treatment.

of 130 units, the second convulsion developed at 9:24 a. m. A third convulsion occurred on the thirty-first treatment day, with a dose of 120 units, at 9:20 a. m. The fourth and last convulsion occurred at 9:54 a. m. on the thirty-seventh treatment day, with a dose of 85 units. In all, the patient had twenty-eight comas, and hypoglycemic shock therapy was terminated July 22 because of fracture dislocation of the left humerus sustained during the last insulin convulsion. His mental condition was much improved and he was discharged from the hospital October 15.

During the course of this investigation the patient was requested to return to the hospital for stereoscopic roentgenograms, which were taken March 25, 1939. These revealed compression fractures and slight wedging of the bodies of the fourth and fifth dorsal vertebrae. Although the patient complained vehemently of pain in the left arm when it was fractured, there was no complaint of back pain (fig. 2).

CASE 23.—N. M., a white youth aged 18, single, was admitted to the Psychiatric Institute Dec. 22, 1933, with a diagnosis of dementia praecox, catatonic type, of three and one-half years' duration. He was thin and fairly well developed, of asthenic habitus, and showed no pathologic condition on physical or laboratory examination. He began hypoglycemic shock therapy Oct. 28, 1936. On the twenty-fourth treatment day, with a dose of 75 units of insulin, the patient had an epileptoid convulsive seizure at 11:50 a. m. A second convulsion occurred on the thirtieth treatment day, with a dose of 50 units, at 11:20 a. m. The third and last convulsion was observed at 11:25 a. m. on the seventy-sixth day of treatment, with a dose of 100 units. In all, the patient had twenty-nine comas, and insulin shock treatment was terminated Feb. 20, 1937, with no observable improvement in the condition.

Metrazol therapy was instituted April 13. The patient had eighteen grand mal seizures, and the maximum dose of metrazol was 6 cc. Treatment was discontinued July 2, the patient being unimproved.

He was removed from the hospital July 5, against advice, and was subsequently admitted to the Kings Park State Hospital, where roentgenograms were obtained April 12, 1939, for this study. These stereoscopic x-ray films showed compression fractures involving the fourth and fifth thoracic bodies, with evidence of bone production over the anterior margins of both vertebrae (fig. 3).

CASE 13.—S. H., a white woman aged 33, married, was admitted to the Psychiatric Institute April 16, 1937, with a diagnosis of dementia praecox, catatonic type, of seven months' duration. She was well nourished, of dysplastic habitus, with some evidence of hypothyroidism. There was no further pathologic physical or laboratory evidence. The patient had three courses of hypoglycemic shock therapy, the first course beginning May 10, 1937, and the last course terminating Dec. 28, 1938. She had improved after the first two courses but had relapsed after a short time. No convulsions occurred during the first two courses, but in the third course on the twelfth day of treatment, with a dose of 135 units of insulin, the patient had an epileptoid convulsion at 10:04 a. m. Stereoscopic roentgenograms of the dorsal spine taken March 22, 1939, revealed no evidence of fracture, injury or abnormality (fig. 4 *A*). The patient manifested no improvement in her mental condition.

Metrazol therapy was instituted March 27, at which time the injection of 5 cc. of a 10 per cent solution of metrazol produced a generalized epileptoid convulsion. Similar convulsions were produced with the same dose March 29 and March 31. Stereoscopic x-ray films of the dorsal spine, taken March 29, revealed compression fractures of the fifth, sixth, seventh and eighth dorsal vertebrae (fig. 4 *B*). During the metrazol treatment the patient was placed in the position of acute flexion, since it was thought that this position would minimize the possibility of fracture. Although she did not actually complain of backache, she was observed clutching her back as if in pain.

SUMMARY AND CONCLUSIONS

1. In a series of 173 patients treated with hypoglycemic shock therapy, sixty-two (36 per cent) manifested epileptoid convulsions.

2. The greatest number of convulsions occurred in the fourth or fifth hour of hypoglycemia.

3. Of thirty-four patients who received only hypoglycemic shock therapy and who were available for roentgenographic examination of the thoracic spine, 20.5 per cent revealed compression fractures of the vertebrae. The incidence was higher in male than in female patients.

4. Of twelve patients treated with both insulin and metrazol who were available for roentgenograms of the spine, three showed compression fractures of the vertebrae.

5. Maintaining the patient in the position of acute flexion while giving metrazol failed to prevent fractures.

6. Two patients with negative x-ray evidence following convulsions during insulin shock therapy subsequently showed compression fractures after metrazol-induced convulsions.

7. A control series of patients with no history of convulsions showed no evidence of injury to the vertebral bodies.

8. The effect of maintaining hyperextension of the spine during metrazol treatment is being investigated.

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RECURRENT LYMPHOCYTIC CHORIOMENINGITIS TREATED WITH SULFANILAMIDE

ISOLATION OF VIRUS

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Lymphocytic choriomeningitis has been recognized as a distinct clinical entity for almost a half century. Wallgren [1] reviewed cases through 1924 and referred to this disease as "acute aseptic meningitis." In 1934 Abramson [2] reviewed cases up to that time. Toomey [3] reported seventy cases in 1936. Dummer, Lyon and Stevenson [4] reported twenty-two cases in 1937. There have also been reports by Gibbens,[5] Gordon and Abrahams,[6] Viets and Watts,[7] Ashton,[8] Mollaret and Kreis,[9] Baird and Rivers,[10] Rodier,[11] Rankin,[12] and

Dr. S. O. Levinson, of the Samuel Deutsch Serum Center, gave helpful suggestions and criticisms.

From the Cook County Contagious Hospital (Drs. Leichenger and Lack), the Department of Pediatrics, University of Illinois College of Medicine (Dr. Leichenger), and the Samuel Deutsch Serum Center, Michael Reese Hospital (Mr. Milzer).

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Ferru.[13] All these reports emphasize the usual features that distinguish this entity. These are the benign course, the symptoms and signs of meningeal irritation, the spinal fluid features of pleocytosis, elevated protein content, and the absence of a bacterial agent. Only in the last five years has the virus nature of this disease been demonstrated by Armstrong and Lillie.[14]

Matturri-Matrai[15] in 1937 reported the case of a 10 year old girl who had two distinct attacks of aseptic meningitis within a period of eighteen days. There was an interval of entire well-being between attacks which lasted eleven days.

In 1937 Cucco[16] reported a case in which there were five distinct attacks over a period of three years. The Olmers and Alliez[17] reported a case which was characterized by a single recrudescence.

In these last three instances no attempt was made to isolate the etiologic agent or to show evidence that neutralizing antibodies were present in the patient's blood serum. In other words, the diagnosis rested entirely on clinical evidence. Skogland and Baker[18] recently reviewed cases of lymphocytic choriomeningitis with sequelae. They reported a case characterized by signs and symptoms of chronic meningo-encephalitis lasting one and one-half years after the initial onset. Neutralizing antibodies were repeatedly demonstrated in the patient's blood. No mention is made, however, of any attempt to recover the virus.

We wish to report a case which we feel is unique in that it was characterized by an initial attack followed by four distinct recrudescences occurring over a period of four months. We also feel that we have adequately demonstrated the presence of the virus of lymphocytic choriomeningitis in the patient's spinal fluid. And finally, we wish to call attention to the fact that sulfanilamide was used in the treatment of this condition with apparent success.

REPORT OF CASE

First Admission.—Initial attack: J. P., a Negro aged 24, born in the United States, admitted to the Cook County Contagious Hospital Oct. 16, 1938, whose past history was of no significance, gave a history of a cough of one year's duration and some weakness, and loss of weight of one month's duration. Headache and stiff neck were present for two weeks before admission. Associated with these symptoms was repeated vomiting for four days prior to entrance to the hospital.

On admission physical examination revealed a temperature of 101.6 F. (rectal), pulse rate 68, respiratory rate 26 per minute and blood pressure 124 mm. of mercury systolic, 78 mm. diastolic. The positive observations were marked neck rigidity and positive Kernig and Brudzinski signs. Laboratory tests were all negative except that the spinal fluid had a ground glass appearance, a 4 plus Pandy reaction and 700 cells per cubic millimeter with 92 per cent lymphocytes. A direct smear and subsequent culture were negative for bacteria, as were results of guinea pig inoculation and special culture for tubercle bacilli. Spinal fluid and blood Wassermann and Kahn reactions were negative. The white cell count showed 12,200 cells per cubic millimeter, of which 68 per cent were of the polymorphonuclear type. The chest roentgenogram was essentially normal.

Our first impression was that we were dealing with tuberculous meningitis, but the subsequent course made this diagnosis untenable. At the Cook County Contagious Hospital all patients with meningitis of undetermined origin are placed on sulfanilamide until the type of meningitis is established. Consequently our patient received 15 grains (1 Gm.) every half hour for six doses and then 15 grains every four hours as a maintenance dose. In three days the temperature dropped to normal, and all objective signs and subjective symptoms disappeared.

Throughout the entire course of the illness, spinal punctures were performed at frequent intervals. The results are shown in the table. These data are fairly consistent. The fluid was opalescent to clear and contained an increase in lymphocytes, the protein was elevated, and chlorides and sugar were at the lower levels of normal. Bacterial cultures, results of guinea pig inoculation for tubercle bacilli and the spinal fluid Wassermann reaction were all negative. The total cell count in the spinal fluid was markedly elevated with each recurrence.

Spinal Fluid Study

	First Admission			Second Admission				Third Admission	
	Initial Attack			First Recurrence		Second Recurrence		Third Recurrence	Fourth Recurrence
Date	10/16/38	10/24/38	10/28/38	11/4/38	11/9/38	11/28/38	12/21/38	1/17/39	1/26/39
Color	Opalescent	Clear	Clear	Opalescent	Clear	Clear	Clear	Opalescent	Opalescent
Pandy reaction	4 plus	4 plus	1 plus	3 plus	2 plus	3 plus	3 plus	4 plus	4 plus
Total cells per cubic millimeter	700	110	70	860	80	238	76	970	846
Lymphocytes, per cent	92	76	96	61	90	70	97	90	100
Sugar, mg. per 100 cc.	...	30	...	37	26	23	...	34	20
Protein, mg. per 100 cc.	...	...	...	...	...	...	...	357	300
Chlorides, mg. per 100 cc.	...	...	...	720	610	...	...	630	670
Culture and smear	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Wassermann and Kahn tests	Negative	...	...	Negative	...	...	...	Negative	Negative

The patient was discharged for the first time October 30, fourteen days after admission, clinically well. The discharge diagnosis was acute serous leptomeningitis.

Second Admission.—First Recurrence: November 4, five days after his first discharge, our patient was again admitted to the Contagious Hospital with the first recurrence. He gave a history of having been well until twenty-four hours before admission, at which time a severe frontal headache developed. Twelve hours later an elevated temperature and a stiff neck were noted. Physical examination at this time revealed a temperature of 104.6 F. The pharynx was slightly injected, neck rigidity was marked, and Kernig and Brudzinski signs were positive. Spinal puncture revealed essentially the same abnormal features that were noted previously and recorded in the table. The spinal fluid at this time contained 860 cells, of which 61 per cent were lymphocytes.

Immediately after admission the patient was placed on a regimen of 30 grains (2 Gm.) of sulfanilamide every four hours for five doses. This medication was repeated the next day, and on the third day the dose was reduced to 15 grains every four hours. At this time the concentration of sulfanilamide in the blood was 13 mg. per hundred cubic centimeters. The patient responded readily to treatment, becoming afebrile

13. Ferru: A propos des méningites aiguës lymphocytaires bénignes, Rev. méd. du centre-ouest **4**: 48-59 (Feb.) 1932.
14. Armstrong, Charles, and Lillie, R. D.: Experimental Lymphocytic Choriomeningitis of Monkeys and Mice Produced by a Virus Encountered in Studies of the 1933 St. Louis Encephalitis Epidemic, Pub. Health Rep. **49**: 1019-1027 (Aug. 31) 1934.
15. Matturri-Matrai, Edvige: A Special Case of Recurrent Lymphocytic Meningitis in a Patient Presenting Paraplegia, Rinasc. med. **14**: 43-47 (Jan. 31) 1937.
16. Cucco, G. P.: Benign Lymphocytic Meningitis of Recurrent Nature, Athena **6**: 421 (Nov.) 1937.
17. Olmer, D.; Olmer, Jean, and Alliez, J.: Méningite aiguë lymphocytaire bénigne à rechutes, Marseille-méd. **1**: 683-686 (May 25) 1932.
18. Skogland, J. D., and Baker, A. B.: An Unusual Form of Lymphocytic Choriomeningitis, Arch. Neurol. & Psychiat. **42**: 507-512 (Sept.) 1939.

on the third day after admission, and on the fifth day the neck rigidity disappeared.

In the interim results of a complete work-up consisting of spinal fluid cultures, repeated blood culture, blood Wassermann test, agglutination tests for typhoid and undulant fever, test of the sedimentation time, x-ray study of the chest, urinalysis and complement fixation test for gonococci were negative.

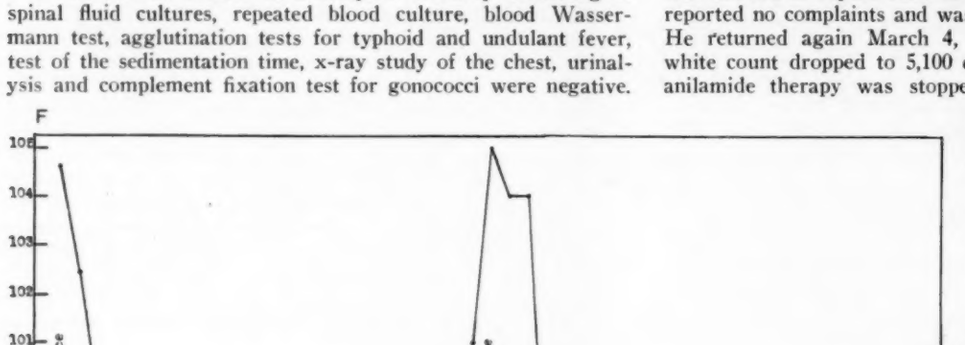

Chart 1.—Temperatures taken daily at 4 p. m. during the second admission.

November 23 sulfanilamide therapy was stopped because of the patient's excellent condition.

Second Recurrence: Five days later, November 28, the patient suddenly became acutely ill. The temperature rose to 105 F. (chart 1), he vomited several times and the stiff neck associated with other objective signs of meningeal irritation reappeared. Spinal puncture at this time showed 238 cells, 70 per cent of which were lymphocytes. Sulfanilamide therapy was reinstituted. In two days he became afebrile, and all physical features gradually became normal. The patient was released for the second time December 23, entirely asymptomatic; he was advised to continue taking 15 grains of sulfanilamide three times a day at home. He was discharged this time with a clinical diagnosis of recurrent lymphocytic choriomeningitis.

Third Admission.—Third Recurrence: This occurred Jan. 16, 1939. He had stopped taking sulfanilamide January 11, five days before admission. He was entirely well until two days before admission, when he noted an elevation in temperature, vomited a few times, became restless and irritable and had slight neck pains. Physical examination at the time of this admission showed a temperature of 102 F., the neck was rigid, and Kernig and Brudzinski signs were positive. The spinal fluid contained 970 cells per cubic millimeter with 90 per cent lymphocytes.

As previously, the patient was given 15 grains of sulfanilamide every four hours. The same satisfactory response was noted at once. Neck rigidity gradually disappeared, and the temperature returned to normal in four days. Five days after admission sulfanilamide medication was stopped.

Fourth Recurrence: Five days after discontinuance of sulfanilamide therapy symptoms again recurred. Neck rigidity developed for the fifth time. The temperature rose to 103 F., and this time there were 846 cells in the spinal fluid, practically all of which were lymphocytes. In order to see if the antipyretic action of sulfanilamide was responsible for the beneficial effects we substituted acetylsalicylic acid. This medication was continued for five days, but the patient's temperature remained elevated. Headache, vomiting, restlessness and neck rigidity persisted. Acetylsalicylic acid treatment was stopped, and sulfanilamide therapy was resumed. In three days all subjective symptoms and objective evidence disappeared (chart 2).

On February 13, seventeen weeks after the initial onset, our patient was entirely well. There were no evidences of any sequelae in the form of mental disturbances or localizing neurologic features. He was discharged with a maintenance dose of 7½ grains (0.5 Gm.) of sulfanilamide three times a day and was advised to report back to the hospital. One week later he reported no complaints and was told to continue the medication. He returned again March 4, feeling well. At this time his white count dropped to 5,100 cells per cubic millimeter. Sulfanilamide therapy was stopped. Our patient remained well and continued working until his last report to the hospital March 28, 1939, at which time contact with him was lost. Our final diagnosis was recurrent lymphocytic choriomeningitis.

ISOLATION OF THE VIRUS

Five cc. of cerebrospinal fluid collected from the patient at the onset of the fourth recrudescence (Jan. 26, 1939, thirteen weeks after the initial attack) were inoculated subcutaneously into guinea pig 3490. Five-tenths cc. which was seeded into aerobic and anaerobic culture mediums and incubated at 37 C. showed no bacteriologic growth after fourteen days.

In a previous publication[19] one of the authors (A. M.) demonstrated that our stock of guinea pigs and white mice were free from latent infection with virus of lymphocytic choriomeningitis through repeated intracerebral inoculations with sterile starch, broth, and normal brain suspension. Furthermore, in the course of another study we had occasion to inoculate some fifty specimens of spinal fluid from various central nervous

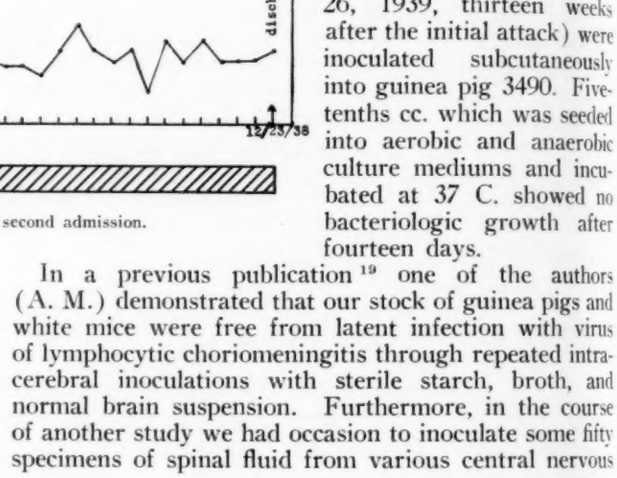

Chart 2.—Temperatures taken daily at 4 p. m. during the third admission.

system infections. Although all these specimens were inoculated in a routine manner subcutaneously into our guinea pigs and occasionally injected intracerebrally into our white mice, none of the animals developed lymphocytic choriomeningitis infection or immunity.

19. Shaughnessy, H. J., and Milzer, Albert: Experimental Infection of Dermacentor Andersoni Stiles with the Virus of Lymphocytic Choriomeningitis, Am. J. Pub. Health **29**: 1103-1108 (Oct.) 1939.

We inoculate guinea pigs subcutaneously as a routine in addition to intracerebral inoculation of white mice for isolating the virus of lymphocytic choriomeningitis because (1) no one has reported activation of a latent infection of this virus by subcutaneous inoculation, and (2) the guinea pig may be readily infected by this route with many known strains. Moreover, we also found as did Traub [20] and Rivers and Scott [21] that guinea pigs are equally susceptible to the intracerebral and the subcutaneous route with the same amounts of virus.

Inoculated guinea pig 3490 had a high temperature (104.2 F.) on the sixth day after inoculation and was found dead after eleven days. This animal had lost 75 Gm. in ten days. At autopsy the brain was intensely hyperemic and diffuse bronchopneumonia was present in the lungs. No bacteria were isolated from the brain tissues or heart's blood of this animal.

The brain was then removed aseptically, and a 10 per cent suspension by weight was prepared in buffered saline solution. Two cc. of this suspension was injected subcutaneously into guinea pig 3491, and 0.03 cc. was injected intracerebrally into each of six white mice. All six inoculated mice had rough coats and coarse body tremors on the sixth day after inoculation. Three of the mice were found dead with characteristic opisthotonos and rigid extension of the hind legs, on the seventh, seventh and eighth days respectively following inoculation. The other three mice recovered and were tested for immunity thirty days after the first inoculation by an intracerebral injection with 0.03 cc. of a 10 per cent suspension of W. E. (Rivers) strain of lymphocytic choriomeningitis virus. The surviving mice were immune to the W. E. strain of virus for the ensuing thirty days, while three control mice inoculated at the same time succumbed in eight days. Histologic examination of the brains of mice and guinea pigs that succumbed to our strain of virus revealed round cell infiltration of the meninges and choroid plexus identical with that produced by the W. E. strain of virus.

Guinea pig 3491 (second passage animal) had a high temperature (104.2 F.) twenty-four hours after the inoculation and was found dead after eight days. This animal had lost 40 Gm. in seven days. At autopsy the brain was hyperemic and other organs were grossly normal. No bacteria were isolated from the brain tissues or heart's blood of this animal.

Virus obtained from guinea pig 3491 was carried through two subsequent passages by further subcutaneous inoculation in guinea pigs. A neutralization test was then carried out using a slight modification of the technic described by Baird and Rivers.[10] Guinea pig 3493 (fourth passage animal) was killed when moribund and its brain was removed aseptically; a 10 per cent suspension by weight in buffered saline solution was prepared and diluted serially to 10^{-5}. Then 0.5 cc. of immune guinea pig lymphocytic choriomeningitis antiserum [22] was mixed with each of the virus dilutions. At the same time control tubes were prepared using normal guinea pig serum plus virus. The mixtures of virus and serum were incubated at 37 C. for one hour. Five-tenths cc. of each dilution was injected subcutaneously into a guinea pig, and the animals were observed for thirty days. All of the guinea pigs which received the immune serum-virus mixtures continued to gain weight, showed no temperature rise and survived, while the control guinea pigs which had received the normal serum-virus mixtures succumbed in nine to ten days with typical signs of lymphocytic choriomeningitis. This evidence that our strain is identical with other known American strains of lymphocytic choriomeningitis virus was confirmed by Dr. Thomas M. Rivers.[23]

We maintained our virus by continued subcutaneous inoculations in guinea pigs. After the tenth passage a titration experiment was carried out to compare the infectivity of our strain with that of the W. E. strain in guinea pigs by subcutaneous inoculation (0.5 cc.) of dilutions ranging from 10^{-1} to 10^{-6}. The W. E. strain had also been maintained in our laboratory by subcutaneous inoculation; it had been passed for fifty-seven generations prior to the titration. Our strain after the tenth passage was decidedly less pathogenic for guinea pigs than the W. E. strain. The former killed in 10^{-4} dilutions, while the W. E. strain killed in 10^{-6} dilutions. A second titration experiment performed after our strain had been passed for twenty-eight generations gave evidence of increased pathogenicity, for at this time it also killed guinea pigs in 10^{-6} dilutions.

To date our strain has been passed for thirty-two generations. It is now 100 per cent fatal for guinea pigs when 0.5 cc. of a 10^{-4} dilution is inoculated subcutaneously. It also kills from 50 to 75 per cent of white mice when given by intracerebral inoculation (0.03 cc. of a 10 per cent suspension).

Filtration experiments have shown that our strain diluted in buffered saline solution (1/20) readily passes through Berkefeld N candles. The infectivity for guinea pigs and white mice has not decreased noticeably after storage for 210 days at 4 C. in a mixture of 9 parts 50 per cent glycerin and 1 part inactivated rabbit serum.

Serum obtained from the patient thirteen weeks after the initial attack was sent to Dr. Charles Armstrong, of the National Institute of Health, for the detection of lymphocytic choriomeningitis antibodies. He reported that he was unable to detect such neutralizing antibodies. A second specimen of serum obtained from the patient seventeen weeks after the onset of the disease (four weeks after the last attack) was sent to Dr. Thomas M. Rivers, who reported that the serum contained neither complement-fixing nor neutralizing antibodies against the virus of lymphocytic choriomeningitis. Unfortunately, we lost contact with our patient and were unable to secure subsequent blood specimens.

COMMENT

From a clinical standpoint our case is of interest for two reasons: first, because of the recurrences; and second, because of the prompt response to sulfanilamide.

The usual case of lymphocytic choriomeningitis is characterized by a single attack of meningeal irritation followed by prompt recovery. Our patient had four distinct recurrences in addition to the initial attack in a period of four months. We have already referred to the report by Skogland and Baker,[18] who reviewed cases characterized by chronicity and neurologic sequelae. This would suggest that the entity of lymphocytic choriomeningitis is more variable in its course than was previously recognized.

The prompt response and apparent control of this malady by the use of sulfanilamide is of unusual interest. One gets the impression from the literature that sulfanilamide and its derivatives are of little value in the

20. Traub, Erich: An Epidemic in a Mouse Colony Due to the Virus of Acute Lymphocytic Choriomeningitis, J. Exper. Med. **63**: 533-546 (April) 1936.

21. Rivers, T. M., and Scott, T. F. McN.: Meningitis in Man Caused by a Filtrable Virus: II. Identification of the Etiological Agent, J. Exper. Med. **63**: 415-432 (March) 1936.

22. The lymphocytic choriomeningitis antiserum was furnished by Dr. Thomas M. Rivers, of the Rockefeller Institute for Medical Research.

23. Rivers, T. M.: Personal communication to the authors.

therapy of the human virus diseases. Rosenthal, Wooley and Bauer [24] found that although sulfanilamide and azosulfamide were ineffective, the original prontosil of Domagk (4-sulfonamide-2,4'-diamino-azobenzene) was effective in the early therapy of lymphocytic choriomeningitis in mice if large doses of the drug and small infective doses of the virus are employed. On the other hand, McKinley, Meck and Acree [25] inoculated mice with large infective doses of the virus and found that azosulfamide was ineffective. They also found that sulfanilamide and sodium sulfanilyl-sulfanilate were inactive against this virus infection.

This patient's course of illness under sulfanilamide is so unusual that we feel that the value of sulfanilamide in the treatment of lymphocytic choriomeningitis deserves further study.

Another unique feature of this case is the isolation of the virus of lymphocytic choriomeningitis from the cerebrospinal fluid thirteen weeks after the initial attack. MacCallum and Findlay [26] report a case in which the virus was still present in the nasopharynx twelve weeks after the onset but not demonstrable in the cerebrospinal fluid at the eighth week. Of course, it is not certain that the initial attack and all of the recrudescences in our patient were lymphocytic choriomeningitis, since no attempt was made to isolate virus prior to the fourth recurrence. However, the similarity of the initial attack and the four recrudescences, both from the laboratory and from the clinical picture, makes it very probable that they all arose from the same causative agent and were recrudescences of the same illness.

The failure to detect complement-fixing and neutralizing antibodies against the virus of lymphocytic choriomeningitis seventeen weeks after the onset of the disease and four weeks after the last recrudescence is not surprising in view of the recurrent course of this malady in our patient. Scott and Rivers [27] have stressed the slow development of antibodies in patients infected with this virus. Howard [28] has reported a case in which antibodies did not appear in the patient's serum for forty-five weeks after onset of the acute infection. More recently, MacCallum and Findlay [26] have reported that they failed to demonstrate neutralizing antibodies in specimens of serum collected from their patient on the ninth, twenty-fourth and fifty-eighth days after illness.

CONCLUSIONS

1. In a case of lymphocytic choriomeningitis lasting over a period of four months there were four distinct recrudescences following the initial attack.

2. Sulfanilamide therapy appeared effective in its control. Approximately 6,797 grains (453 Gm.) was given to this patient without ill effects.

3. The virus of lymphocytic choriomeningitis was isolated from the spinal fluid.

4. Neutralizing and complement-fixing antibodies were not detected in the patient's blood four weeks after the last recrudescence.

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24. Rosenthal, S. M.; Wooley, J. B., and Bauer, Hugo: Studies in Chemotherapy: Chemotherapy of Choriomeningitis Virus Infection in Mice with Sulfonamide Compounds, Pub. Health Rep. **52**: 1211-1217 (Sept. 3) 1937.

25. McKinley, E. B.; Meck, J. S., and Acree, E. G.: Chemotherapy in Virus Diseases, J. Infect. Dis. **64**: 36-42 (Jan.-Feb.) 1939.

26. MacCallum, F. O., and Findlay, G. M.: Lymphocytic Choriomeningitis: Isolation of the Virus from the Nasopharynx, Lancet **1**: 1370-1378 (June 17) 1939.

27. Scott, T. F. McN., and Rivers, T. M.: Meningitis in Man Caused by a Filtrable Virus: I. Two Cases and the Method of Obtaining a Virus from Their Spinal Fluids, J. Exper. Med. **63**: 397-414 (March) 1936.

28. Howard, M. E.: Lymphocytic Choriomeningitis: A Discussion of Its Diagnosis in Man, J. Infect. Dis. **64**: 66-77 (Jan.-Feb.) 1939.

THE SYNTHETIC ESTROGEN STILBESTROL

CLINICAL AND EXPERIMENTAL STUDIES

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The estrogens in general use at present are estrone, estriol and estradiol, all of which are prepared primarily from pregnant mare's urine. These preparations are undeniably potent and clinically effective but have certain practical disadvantages: (*a*) They are expensive, (*b*) they are relatively ineffective orally and (*c*) they are difficult to prepare and, except when prepared in pure crystalline form, must be biologically standardized. A cheaper, orally effective, synthetic preparation which could be administered by weight is greatly to be desired.

The synthesis of a new estrogen which seemed to meet these criteria was announced by Dodds and his co-workers [1] in 1938. It was named diethylstilbestrol because it was derived from stilbene, contained two ethyl groups and was estrogenic. It does not contain the phenanthrene ring nucleus previously thought necessary for estrogenic activity. Preliminary animal studies revealed not only that it was approximately two and one half times as potent as estrone by injection but that it lost little of its potency when given by mouth. No toxic effects were noted in the early animal work.

Clinical trials of stilbestrol (the name adopted to designate diethylstilbestrol) have resulted in uniform agreement concerning its estrogenic effects but considerable disagreement concerning its toxicity. In Winterton and MacGregor's [2] series of fifty-one women, menopausal symptoms were relieved. Nausea was caused in only a few cases. Bishop, Boycott and Zuckerman [3] obtained similar good effects, but three of their forty-three patients complained of nausea and vomiting. Varangot [4] observed nausea and vomiting in eight of eighteen women. In this country preliminary reports on the clinical and toxic effects of the drug have been published by Shorr, Robinson and Papanicolaou,[5] by Buxton and Engle [6] and by us.[7] Shorr and his co-workers found that thirty-five of forty-four women (80 per cent) had toxic symptoms in the form of nausea, vomiting, abdominal distress, anorexia, lassitude, paresthesias, vertigo, thirst, an acute psychotic reaction or cutaneous rashes. Liver function tests could not be considered conclusive but suggested hepatic impairment. The doses used ranged from 0.5 to 5 mg. daily, treatment being continued for from four to seventy-eight

From the Department of Medicine, Washington University School of Medicine, the Washington University Clinics, and the St. Louis City Hospital.

1. Dodds, E. C.; Goldberg, L.; Lawson, W., and Robinson, R.: Estrogenic Activity of Certain Synthetic Compounds, Nature, London **141**: 247 (Feb. 5) 1938.

2. Winterton, W. R., and MacGregor, T. N.: Clinical Observations with Stilbestrol (Diethylstilbestrol), Brit. M. J. **1**: 10 (Jan. 7) 1939.

3. Bishop, P. M. F.; Boycott, Muriel, and Zuckerman, S.: Estrogenic Properties of "Stilbestrol" (Diethylstilbestrol): Clinical and Experimental Investigation, Lancet **1**: 5 (Jan. 7) 1939.

4. Varangot, J.: Activé oestrogène et toxicité du stilboestrol (4: 4 dihydroxy alpha beta diethylstilbene), Presse méd. **38**: 725 (May 13) 1939.

5. Shorr, Ephraim; Robinson, F. H., and Papanicolaou, G. N.: A Clinical Study of the Synthetic Estrogen Stilbestrol, J. A. M. A. **113**: 2312-2318 (Dec. 23) 1939.

6. Buxton, C. L., and Engle, E. T.: Effects of Diethylstilbestrol Therapy, J. A. M. A. **113**: 2318-2320 (Dec. 3) 1939.

7. MacBryde, C. M.; Freedman, Harold, and Loeffel, Ellen: Studies on Stilbestrol, J. A. M. A. **113**: 2320 (Dec. 3) 1939.

days. Buxton and Engle found no evidence of toxicity in sixteen of seventeen cases. Albumin and casts were found in the urine in one case, possibly attributable to the drug. In our own series, as recorded in our preliminary report, nausea occurred in eight of thirty-seven patients, vomiting in three.

In this paper we propose to give a more complete report of our clinical and experimental studies of the effects of stilbestrol.[7a]

CLINICAL MATERIAL AND METHODS

Studies were started in March 1939. Fifty-six women have been treated. Of these, fourteen have had both ovaries removed, nine have had part of the ovarian tissue removed, five were eunuchoid young women with amenorrhea and twenty-eight were suffering with symptoms of spontaneous menopause. Two criteria of selection of cases were employed: (1) symptoms severe and characteristic of hypo-ovarianism and (2) vaginal smears definitely of the inactive, castrate type. Patients have been given stilbestrol constantly for periods ranging from two weeks to eight months. Eighteen of the fifty-six have received stilbestrol constantly for six months or longer.

The dose has ranged from 0.1 to 5 mg. daily of stilbestrol dipropionate by mouth or intramuscularly in oil. The average dose has been 1 mg. daily and thirty-one of our patients are now maintained on this dose orally. The largest doses have been given two patients with primary hypogonadism. Each of them received slightly over 700 mg. intramuscularly in 180 days.

Vaginal smears were made at intervals, twice a week at first, later once a week and then once every two weeks. The dose necessary to obtain and maintain full estrous response was determined in each case. Subjective responses were analyzed as carefully as possible and an attempt was made to correlate the subjective and objective results and relate them to the dosage. Endometrial biopsies were made before and after treatment in eight cases.

On all patients receiving large doses over considerable periods of time, repeated tests of liver function, red blood cell and white blood cell counts, hemoglobin determinations, differential white cell counts and blood platelet counts were performed. Loeser [8] has observed anorexia, vaginal and intestinal hemorrhage and liver cell degeneration in rats given large doses. Tislowitz [9] found granulocytopenia and anemia in dogs receiving 5 mg. daily by injection for from twenty-five to fifty days. Morrell [10] has shown no pathologic changes in tissues of rats, rabbits or monkeys. We [11] have found that both stilbestrol and natural estrogens in large dosage will produce anemia, thrombocytopenia and hemorrhage, as well as hypoplastic changes in the bone marrow of dogs.

In addition to the tests of liver function, repeated examinations of the urine have been done.

Two tests of liver function were used—bromsulphalein excretion and hippuric acid synthesis. In addition, the icterus index was determined at intervals and the prothrombin time measured.

7a. Stilbestrol for these studies was supplied to us by Dr. J. B. Rice, of the Medical Research Department, Winthrop Chemical Company.

8. Loeser, Arnold: Untersuchungen über die Pharmakologie und Toxicologie synthetischer Bruntstoffe, Ztschr. f. d. ges. exper. Med. **105:** 430 (April) 1939; Klin. Wchnschr. **18:** 346 (March 11) 1939.

9. Tislowitz, R.: Acta brev. Neerland **9:** 15, 1939.

10. Morrell, J. A.: Endocrinology, to be published.

11. MacBryde, C. M.; Castrodale, Dante; Helwig, A. B.; Bierbaum, O., and Poe, J., to be published.

RESULTS

1. *Subjective Effects.*—Definite relief of hypogonadal symptoms was obtained in fifty-two of the fifty-six cases. The degree of relief varied from excellent in thirty-five cases to fair in seventeen cases. Hot flashes were decreased in all cases in which they were a prominent complaint. Headache was relieved in sixteen of twenty-one cases in which it had been severe. A tendency to nausea and vomiting was decreased in four cases. Energy seemed greater in twenty-eight of thirty-two patients who had complained of lassitude. Pruritus vulvae was relieved in eight of nine cases. Increased sexual desire was reported by twelve patients. These effects were in general similar to those we have previously seen with large doses (from 10,000 to 30,000 rat units weekly) of estradiol benzoate.

Untoward subjective effects occurred in nine of our fifty-six cases (16 per cent), consisting of slight nausea in five cases and of nausea and vomiting in four cases. In two of the four cases with vomiting the drug was later resumed, the dose being reduced from 5 mg. intramuscularly three times a week to 1 mg. by mouth daily, and nausea did not recur. In the other two cases the patients would not try the drug again.

No other untoward effects were observed. We had no patients who complained of abdominal distress or lassitude or who had cutaneous rashes or diarrhea.

2. *Objective Effects.*—The vaginal smears, which in all cases were of the inactive castrate type before treatment, showed active estrous changes under stilbestrol therapy. Within four days after 5 mg. intramuscularly the smears showed marked changes and in seven days the change was that of complete estrous response. After 1 mg. daily by injection the change was usually partial in seven days and complete in fourteen days. When given by mouth, 1 mg. daily takes on the average twenty-one days to cause the complete response.

After full vaginal smear changes were obtained at any dosage level and treatment was stopped, it took from twenty-one to thirty days for the smear to regress gradually to the castrate type. Symptomatic relief followed roughly the vaginal smear picture. Patients, however, frequently felt better before full estrus was reached and usually felt worse within one week after the drug was stopped, even though the vaginal smears might still appear quite active.

The endometrial biopsies revealed active proliferative changes after 10 mg. intramuscularly given in seven days, or after 20 mg. orally in fourteen days.

From the subjective and objective effects on our patients, stilbestrol would seem to be from 50 to 66 per cent as effective by mouth as by injection. The oral route seems more apt to cause nausea in susceptible patients but otherwise seems the route of choice.

Stilbestrol is considerably more active than estrone (theelin), the most widely used of the estrogens. A number of our patients had previously been treated with estrone, and some of them have since received courses of estrone for comparison with the stilbestrol effect. It is necessary to compare the same patient when making such a parallel study, a point which is evident when it is found that complete symptomatic relief and estrous changes were brought about in two cases only after 5 mg. daily by injection for approximately fourteen days, while at the other extreme 1 mg. daily by mouth has maintained a positive smear in several cases for months. In one case of a menopausal patient in which such a comparison can be made, 1 mg. of estrone (10,000

international units) three times a week by intramuscular injection was more than equaled objectively and subjectively by 0.5 mg. of stilbestrol daily by mouth. A patient with primary hypogonadism showed regression of smears and breast atrophy when given less than 1 mg. (10,000 international units) of estrone daily. Stilbestrol, 1 mg. by injection three times a week, caused breast growth and active vaginal changes. From these observations it would seem that stilbestrol dipropionate is more than twice as active per milligram as estrone when given intramuscularly and that a milligram of stilbestrol orally is approximately equivalent to a milligram of estrone by injection.

As compared with estradiol benzoate, similar observations in four cases have led us to conclude that stilbestrol is approximately one third to one half as potent when given by intramuscular injection.

An effective way to administer stilbestrol is by subcutaneous implantation of hard pellets of the pure crystalline drug, as we have described.[12] By extracting and weighing such pellets at intervals, a pellet of approximately 100 mg. is found to be absorbed at a rate ranging from 0.127 to 0.250 mg. a day. Symptomatic improvement and positive changes in the vaginal smears have been maintained for from four to seven months by eight castrate patients in whom one pellet has been implanted. Whether or not continuous therapy in such small doses by pellet implantation is preferable to oral therapy with larger doses, which can however be interrupted at intervals, is not yet determined.

All of our patients with small breasts receiving large doses of stilbestrol had breast growth of a degree sufficient to be measurable. Larger doses are required to produce progressive breast growth than are necessary to maintain estrous changes in the vaginal smear. Other patients noticed some sensitivity and tenseness of the breasts, with enlargement of the nipples and pigmentation of the areolae.

Uterine bleeding was produced in fourteen of the fifty-six cases. In ten of the fourteen cases this bleeding occurred after discontinuance of the drug, beginning from four to ten days later and lasting from three to fourteen days. In the remaining four cases bleeding started during treatment with the drug. Treatment was stopped in each case a few days after the bleeding started. In one case it lasted eight days, in one eleven days, in one twenty-three days and in one thirty-two days. In the last two cases cessation followed injections of progesterone. Endometrial biopsy showed a hypertrophic endometrium in the last case.

STUDIES OF TOXICITY

1. *Liver Function Studies.*—Twenty-six patients who had received the largest doses and had been treated for the longest periods had liver function studies performed, both by the bromsulphalein excretion and by the hippuric acid synthesis test. In six cases the tests were performed before any treatment was given and again after periods of from thirty to ninety days, during which amounts varying from 30 to 250 mg. had been given. The average daily dose in this group was 2 mg. daily, the minimum 1 mg. daily. In no case was there any significant change by either of the liver function tests.

In twenty cases the studies were not performed before the drug was started but after stilbestrol had been given for some time. Totals of from 120 to 700 mg. had been given in from 120 to 180 days. Bromsulphalein excretion and hippuric acid synthesis were well within normal limits in all these cases.

Icterus index determinations were normal in all nineteen cases in which they were done and did not rise during continuous stilbestrol therapy.

2. *Blood Studies.*—No abnormalities were noted in total red blood cell counts, white blood cell counts, differential counts or platelet counts. No tendency to hemorrhage was observed in the skin or mucous membranes. The only bleeding produced was the uterine bleeding previously described. In none of the cases of prolonged bleeding was any abnormality of the blood noted except in the case in which the longest period of bleeding occurred. Here there was a slight fall in the red blood cell count and hemoglobin content, which returned to normal within two weeks after the bleeding ceased.

3. *Urine Studies.*—No urinary abnormalities occurred in twenty-two cases in which repeated urine examinations were made while under treatment for from two to eight months.

COMMENT AND SUMMARY

We have endeavored to judge the therapeutic and toxic effects of stilbestrol dipropionate when administered to fifty-six women suffering from severe hypogonadism. The results from the therapeutic standpoint are excellent, great relief of the symptoms of primary hypogonadism, of castration and of the menopause being obtained by thirty-five of fifty-six patients (62 per cent) and fair or partial relief by seventeen (30 per cent).

Nine patients (16 per cent) had unpleasant effects such as nausea and vomiting. The nausea occurred after injection therapy as well as after oral administration and cannot be considered due to direct gastrointestinal irritation. Reducing the dose or changing from oral to injection treatment reduces the tendency to nausea and was successful in all but two of our cases. In these two the stilbestrol treatment was discontinued.

It is important to determine whether the nausea and vomiting are evidence of more serious functional or organic disturbance or whether they may be considered relatively innocuous. Previous studies, both clinical and experimental, have given widely divergent results. Our results, as compared with those of Shorr, Robinson and Papanicolaou, show a much smaller percentage of untoward effects. Although the liver function studies which we performed showed no reason to suspect liver damage from the dosage employed, too much reliance cannot be put on such functional tests, as it is well known that minor hepatic impairment may be present without significant alteration.

Studies in our own laboratories [11] have shown that in dogs and rats receiving stilbestrol in doses comparable to the very highest therapeutic doses anemia and thrombocytopenia result. In animals receiving much larger doses, severe thrombocytopenia with hemorrhages and death may occur. However, we have also demonstrated similar results with comparable doses of estradiol benzoate, so that at present it seems doubtful whether in this respect there is any difference between the toxic effects of natural and of synthetic estrogens.

CONCLUSIONS

1. Stilbestrol dipropionate gave excellent subjective relief to thirty-five of fifty-six hypogonad women (62 per cent) and partial relief to seventeen (30 per cent).

2. It is a highly potent estrogen, producing estrous vaginal smears, proliferative changes in the endometrium, breast growth and all the other known effects of natural estrogens.

12. MacBryde, C. M.; Freedman, Harold; Loeffel, Ellen, and Allen, Duff: Estrogenic Therapy by Implantation of Stilbestrol Pellets, Proc. Soc. Exper. Biol. & Med. **43**: 212-214 (Jan.) 1940.

3. Compared to estrone, stilbestrol is approximately twice as potent when given intramuscularly. A milligram of stilbestrol orally is roughly equivalent to a milligram of estrone intramuscularly.

4. By intramuscular injection, stilbestrol is approximately one third to one half as potent per milligram as estradiol benzoate.

5. Stilbestrol is roughly from 50 to 66 per cent as potent orally as by injection.

6. Nine patients (16 per cent) had unpleasant effects, consisting of nausea in five instances and of nausea and vomiting in four. In only two cases was it necessary to discontinue the drug. In no case were serious results detected. No abdominal distress, diarrhea or cutaneous rashes occurred.

7. Studies of liver function showed no evidence of hepatic impairment. No changes were noted in the blood or urine.

8. Further studies of stilbestrol and related compounds are indicated before these substances are released for general use. The toxic effects of the natural and of the synthetic estrogens should be compared, since it has been demonstrated that in high dosage both may be toxic.

600 South Kingshighway.

TESTICULAR TUMORS IN MICE RECEIVING ESTROGENS

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AND
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During the course of prolonged high estrogen treatment the glandular interstitial tissue of the testis in mice of the Strong A strain has been observed to hypertrophy, in a few instances to such an extent that large areas of the testis were composed entirely of these cells.[1] Since neither local invasions nor metastases were observed, not one of these hypertrophies or overgrowths was considered malignant. Recently, however, a malignant tumor of the interstitial cells appeared in an A strain mouse receiving estradiol benzoate.

This mouse had received weekly subcutaneous injections of 0.05 mg. of estradiol benzoate [2] in sesame oil beginning at the age of 30 days. Shortly after six months of treatment the left testis began to increase in size rather rapidly, and after eight months it was several times normal size, was nodular and protruded somewhat above the base of the tail. Shortly thereafter the general health of the animal appeared to decline, and it was killed for study 264 days after the start of treatment.

As shown in figure 1, the left testis was much enlarged, weighing 1.03 Gm.; it was brown and irregularly spherical. The tunica albuginea exhibited surface irregularities, and the epididymis was distorted and firmly adhered to the tunica. Microscopically this testis contained only an occasional remnant of a tubule and was composed almost entirely of cords and masses of large vacuolated cells resembling the hypertrophied interstitial cells previously described [1] (fig. 2). Many of these cells were atypical in that they were multinucleated or contained finely granular basophilic nuclear inclusions. Although fat stains were not employed, the vacuolated character of the cytoplasm indicated a high lipoid content. Mitotic figures were frequently encountered in these tumor cells. The tunica albuginea was extensively invaded and in places almost obliterated. The few remaining tubules were atrophic, the least degenerated of them containing Sertoli cells and spermatogonia or only Sertoli cells. Other tubules were entirely empty and frequently were represented only by sinusoid-like spaces.

The lumbar lymph nodes were greatly enlarged, as shown in figure 1, and the left node was the color of the left testis. The metastatic involvement of this node was so extensive that its lymphoid structure was lost, its chief component being the large vacuolated cells characteristic of the primary testicular lesion (fig. 3). The right lumbar node was normal in color and the metastatic involvement was limited primarily to the peripheral sinuses. A left renal node was similarly enlarged, brown, and infiltrated much the same as the left lumbar node. No other metastases were seen.

Fig. 1.—Mouse which received estradiol benzoate. The tumor of the left testis (LT) is 1.4 cm. in diameter and nodular. The right testis (RT) is hypertrophied, but to a lesser extent. The seminal vesicles (SV) are approximately two-thirds normal size. The lumbar lymph nodes (LN) are greatly enlarged.

The right testis (weight 0.175 Gm.) was of normal shape and, although distinctly enlarged, it was much smaller than the left testis. It also was composed chiefly of large vacuolated interstitial cells which widely separated the tubules. The histologic features of this testis indicated the existence of a marked diffuse hyperplasia which did not, in our opinion, represent a metastasis from the other testis. The tubules of the right testis were less severely damaged than those of the left and occasionally contained spermatocytes.

The accessory organs of reproduction, as is usual in estrogen-treated mice, exhibited increase in their fibromuscular tissue components. The extent of the expected estrogen effect was modified, however. The seminal vesicles were approximately two-thirds normal size, contained some secretion and were lined by a tall columnar epithelium almost identical with that of an untreated male or of a male receiving androgens. The lining epithelium of the coagulating glands was columnar rather than stratified squamous as usually seen after treatment with estrogens. The prostatic epithelium was essentially normal, as was the epithelium of the ejaculatory ducts and the prostatic urethra. The myxomatous

From the Department of Anatomy, Yale University School of Medicine. This study was aided by grants from the Fluid Research Fund of Yale University School of Medicine, the Anna Fuller Fund, the Jane Coffin Childs Memorial Fund for Medical Research, and the Committee for Research in Problems of Sex of the National Research Council.

1. Gardner, W. U.: Hypertrophy of Interstitial Cells in the Testes of Mice Receiving Estrogenic Hormones, Anat. Rec. **68**: 339 (June) 1937.

2. The estradiol benzoate was supplied by the Schering Corporation through Drs. E. Schwenk and Max Gilbert.

changes of the connective tissue of the ejaculatory ducts characteristically elicited by estrogen were lacking. The observations indicate that these tissues were under the influence of androgen, suggesting the possibility of endocrine activity of the hypertrophied and malignant cells.

Various abnormalities, usually seen in estrogen-treated mice,[3] were also present in this animal. The bladder was greatly distended, the ureters and renal pelves were dilated and the kidneys were enlarged. The bile ducts were modified, and the marrow cavities of the long bones were obliterated by endosteal deposits of new bone. The pubic symphysis was replaced by a ligament 1 mm. in length. The adrenals and the hypophysis, however, appeared normal.

A large tumor of the glandular interstitial cells also developed in one mouse of the A strain which received 250 micrograms of stilbestrol [4] weekly from the thirty-sixth to the two hundred and eightieth day of life. This tumor was slightly smaller, measuring 10 mm. in diameter, but was almost identical histologically (fig. 4) with the tumor already described. No metastases were

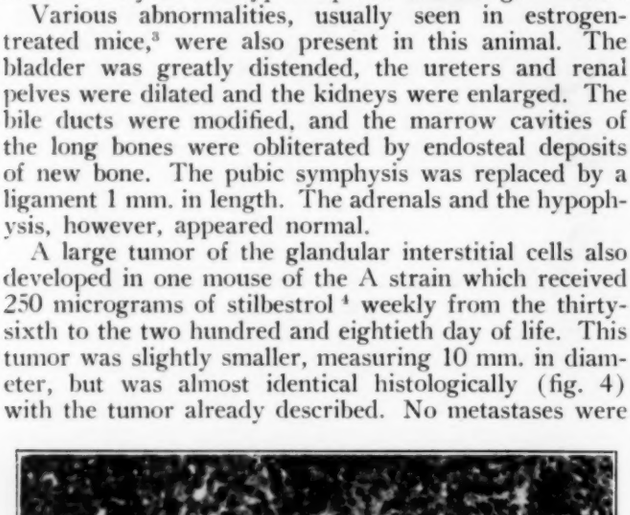

Fig. 2.—Section of an area of the testicular tumor of the mouse shown in figure 1; × 110.

discovered, however, and its malignancy is unproved. The other testis of this animal again showed marked interstitial cell hypertrophy and the accessory genital organs manifested signs of androgen stimulation similar to those enumerated for the other animal.

Thus far, testicular tumors have not been observed in this laboratory to arise spontaneously in mice of the A strain, although the number of old males examined has perhaps been too small definitely to exclude the possibility of rare spontaneous origin. Moreover, tumors of the testis have not appeared in mice of other inbred strains receiving estrogens. Indeed, only mice of the A strain have responded to estrogens with interstitial cell hypertrophy.[1] Burrows,[5] however, has reported rather a high incidence of Leydig cell hypertrophy in stock mice receiving estrogens.

3. Allen, E.; Hisaw, F. L., and Gardner, W. U.: The Endocrine Functions of the Ovaries, chapter VIII in Allen, Edgar; Danforth, C. H., and Doisy, E. A.: Sex and Internal Secretions, Baltimore, Williams & Wilkins, 1939.

4. The stilbestrol was supplied by E. R. Squibb & Sons through Dr. J. A. Morrell.

5. Burrows, Harold: A Comparison of the Changes Induced by Some Pure Estrogenic Compounds in the Mammae and Testes of Mice, J. Path. & Bact. **42**: 161 (Jan.) 1936; Acquired Resistance to Estrone in a Male Mouse, ibid. **44**: 699 (May) 1937.

The sequence of changes in the testis recalls that seen in the mammary glands, cervix uteri and hypophysis of estrogen-treated mice [6] in that it consists of a hypertrophy of the affected element (in this case the interstitial cells) by increase in both size and number

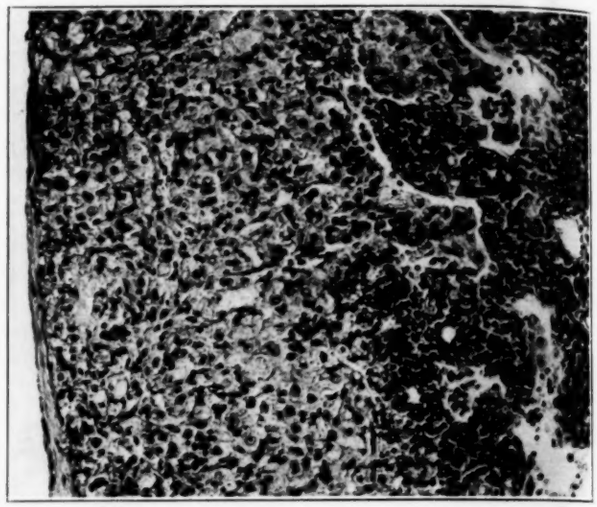

Fig. 3.—Section of the metastasis of the testicular tumor to a lumbar lymph node; × 195.

of cells followed by diffuse hyperplasia and finally malignancy. The testicular changes bear further general resemblance to the changes in the mammary glands, cervix and hypophysis in their appearance following chemically different estrogens and in their limitation by factors inherent in the strain of mice.

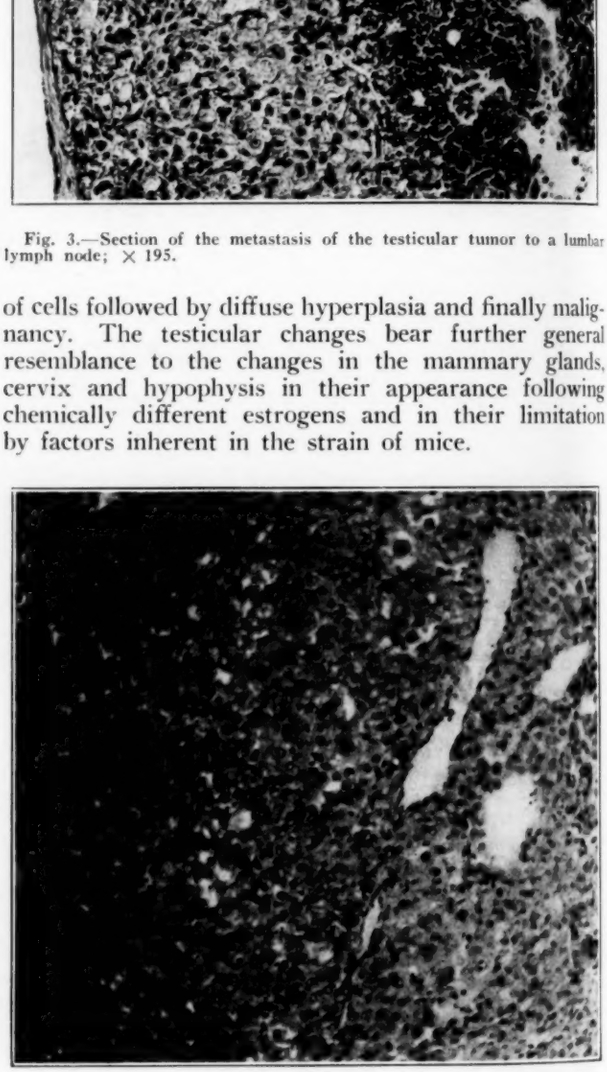

Fig. 4.—Section of the testicular tumor of the mouse receiving stilbestrol; × 100.

SUMMARY

A large interstitial cell tumor of the testis which metastasized to the lumbar and renal lymph nodes developed in a mouse of the A strain receiving estradiol benzoate over a period of 264 days. A histologically

6. Gardner, W. U.: Estrogens in Carcinogenesis, Arch. Path. **27**: 138 (Jan.) 1939. Lacassagne, A.: Les rapports entre les hormones sexuelles et la formation du cancer, Ergebn. d. Vitamin- u. Hormonforsch. **2**: 259, 1939.

similar testicular tumor which did not metastasize also arose in a second mouse of the same strain receiving stilbestrol. The histologic picture of the accessory organs of reproduction in both instances indicates that these tumors secreted androgenic material.

333 Cedar Street.

Clinical Notes, Suggestions and New Instruments

CHRONIC CONJUNCTIVITIS DUE TO THE VIRUS OF VENEREAL LYMPHOGRANULOMA

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Under the name Parinaud's conjunctivitis a peculiar inflammation of the conjunctiva of one eye with subsequent swelling of the regional preauricular and submaxillary lymph glands has been described. The various organisms that have been accused as possible causative agents include the tubercle bacillus (human and bovine), Bacterium tularense, Spirochaeta pallida, the glanders bacillus, Sporothrix, Streptococcus and Leptothrix. The virus of venereal lymphogranuloma has also been listed among the etiologic organisms.

In this paper we are adding to the small number of recorded cases another case of conjunctivitis due to the virus of venereal lymphogranuloma.

The French ophthalmologist Morax [1] was the first author to call attention to the etiologic relationship of the virus of venereal lymphogranuloma to some cases of Parinaud's conjunctivitis, although he had no case of his own to prove his point. In the case of Levaditi, Bollack, Basch and Desvignes,[2] marked unilateral conjunctivitis of the bulb and lids and swelling of the preauricular and submaxillary glands occurred in a man aged 37. Material from an extirpated lymph node of the patient inoculated intracerebrally into a monkey produced a characteristic meningitis. Changes compatible with venereal lymphogranuloma were also evoked in mice by injection of the monkey brain emulsion. Further subpassages into mice were not successful. Frei tests with emulsions of the monkey and mouse brains as well as material from the preauricular glands of the patient gave positive reactions. Another case was that occurring in a woman physician [3] at the Institute of Bacteriology of Louvain, Belgium, who had worked with the virus. Unilateral conjunctivitis and later preauricular and submaxillary lymphadenitis and parotitis with fever developed. The Frei reaction was positive. Causes other than venereal lymphogranuloma could be ruled out.

Similar involvement of the regional lymph nodes developed in Ichijo's [4] case of unilateral conjunctivitis. In his and in Weidman's [5] case, in which conjunctivitis was characterized by marked edema, genital manifestations of venereal lymphogranuloma preceded the involvement of one eye.

Experimentally, successful inoculations of the virus of venereal lymphogranuloma into the conjunctiva of chimpanzees with production of a characteristic conjunctivitis were performed by Levaditi, Schoen and Reinié.[6]

REPORT OF CASE

C. G., a white man aged 39,[7] was presented at the December 1938 meeting of the New York Academy of Medicine, section of Dermatology, with the diagnosis of chronic conjunctivitis of the right eye, probably due to the virus of venereal lymphogranuloma. This diagnosis has been confirmed by further study.

In 1926 the patient had gonorrhea which did not involve his eyes. In 1930 he had a generalized rash of secondary syphilis, the Wassermann reaction being 4 plus. At that time and subsequently he received adequate treatment with the arsphenamines, heavy metals and large doses of potassium iodide. This management led to a negative Wassermann reaction of the blood and to absence of signs and symptoms of syphilis but did not in the least influence a condition of the right eye which had developed during May 1932 and has persisted ever since. In 1935 he was operated on for anal fistula at Bellevue Hospital. At that time the clinical appearance of the rectum was not suggestive of venereal lymphogranuloma. A Frei test was not performed.

In May 1932, after perverted intercourse with a Negress, conjunctivitis of the right eye developed. The right preauricular and submaxillary nodes became swollen and tender. Agglutination tests for Bacterium tularense were done twice and were negative. Tuberculin tests with dilutions of 1:100,000 and 1:10,000 gave negative results. Guinea pigs injected with macerated tissue from the conjunctiva remained well after eight days. Cultures of material from the eye yielded staphylococci or Bacillus xerosis or were sterile. A specimen of the eye was taken for biopsy on which the diagnosis was chronic granuloma. In December 1932 the patient was presented by Dr. Abraham Fine [8] before the Section of Ophthalmology of the New York Academy of Medicine. No definite diagnosis of the condition of the eye was made at that time. Until 1933, treatment at various times had consisted of injections with milk, roentgen and radium irradiation and topical applications, all without result. No more treatment was then attempted until 1938.

Fig. 1.—Conjunctivitis of right eye in November 1938.

When seen at the Vanderbilt Clinic in November 1938, the right eye showed swelling and inflammation of both lids, with considerable edema, especially of the lower lid, and some purulent conjunctival discharge. There was marked destruction of the inner surface of the lids. The right globe was intensely injected. The cornea was opaque (fig. 1). Vision had been lost since 1933. At no time did the patient complain of pain in the eye.

There was no longer enlargement of any of the lymph nodes. General examination revealed no abnormality, and there were no signs of past or present venereal disease visible on the genitals or in the inguinal areas. Proctologic examination revealed a scar from an operation for anal fistula. In the opinion of the proctologist (Dr. C. V. Burt) there was nothing present to suggest venereal lymphogranuloma of the rectum.

Repeated Frei tests with reliable human antigens were strongly positive. A cutaneous test for chancroid (Ducrey's bacillus vaccine, Lederle) was doubtful (0.4 cm. slightly infiltrated redness).

From the Department of Dermatology and the Department of Bacteriology, Columbia University College of Physicians and Surgeons.

1. Morax, V., cited by Bollack, J.: Bull. soc. franç. de dermat. et syph. **43**: 1243 (June) 1936.
2. Levaditi, C.: Bollack, J.; Basch, G., and Desvignes, P.: Bull. soc. franç. de dermat. et syph. **43**: 1238 (June) 1936.
3. Ronse, Marguerite: Ann. de la soc. belge de medicine tropicale **18**: 639 (Dec. 31) 1938. Bollack, J.; Basch, G., and Desvignes, P.: Bull. soc. ophth. **5**: 409, 1936.
4. Ichijo, Morinasa: Act. soc. ophth. Jap. **41**: 628 and 1487, 1937.
5. Weidman, F. D., in discussion of Weidman, F. D., and Hunter, Robert: Lymphogranuloma Inguinalis, Arch. Dermat. & Syph. **34**: 342 (Aug.) 1936.
6. Levaditi, C.; Schoen, Rachel, and Reinié, Louis: Compt. rend. Acad. d. sc. **203**: 828 (Oct. 26) 1936.
7. Hopkins, J. G.: Chronic Conjunctivitis of the Right Eye, Probably Due to the Virus of Lymphogranuloma Venereum, Arch. Dermat. & Syph. **39**: 742 (April) 1939.
8. Fine, Abraham: An Obscure Disease of the Conjunctiva Simulating Parinaud's Conjunctivitis, Arch. Ophthal. **9**: 677 (April) 1933.

The serum protein value was 7.4 per cent, albumin 4.7 per cent and globulin 2.7 per cent.

Biopsy of the lid (Jan. 17, 1939) showed a fragment of conjunctival epithelium which in areas was infiltrated with polymorphonuclear cells. The major portion of the specimen was made up of very vascular granulation tissue. The numerous blood vessels were separated by masses of cells which were almost exclusively plasma cells. In places these were densely packed, in others separated by edema. In the latter areas there was considerable admixture of polymorphonuclear neutrophils. The walls of many of the small vessels were edematous and infiltrated with neutrophils. Many eosinophils and neutrophils were seen in the lumen of the vessels. No definite diagnosis as to the nature of the granuloma was possible.

Results of Cutaneous Tests with Various Materials Prepared as Antigens

Material	Cutaneous Reactions in Known Cases of Venereal Lymphogranuloma with Previous Positive Frei Tests (Human Antigens)	Cutaneous Reactions in Control Cases with Previous Negative Frei Tests (Human Antigens)
A. Filtered washings of eye...	−	−
	−	−
	−	−
B. Tissue culture (inoculated with A unheated)	+	−
	+	−
	+	
	+	
C. Tissue culture control.....	−	−
	−	−
		−
D. Brain of mouse inoculated from tissue culture	+	
E. Biopsy from eye *.....	+	−
	+	
	+	

* When injected previous to heating into monkey, produced transitory symptoms and cerebral changes, verified microscopically.

Four intravenous injections of Frei antigen were given without definite effect on the lesion of the eye. The first two injections caused systemic febrile reactions. The patient was then given sulfanilamide in doses of 80 and 60 grains (5 and 4 Gm.) a day. After a total of 540 grains (32.4 Gm.) less infiltration of the eyelids was noted. After continued treatment with sulfanilamide, which he took irregularly for four months, improvement of the eye progressed to a relatively satisfactory state (fig. 2). Five months after discontinuance of the drug Dr. Thygeson, the ophthalmologic consultant, stated "There is no evidence of ocular activity at present. The lids are adherent to the globe. The cornea is keratinized. There is no discharge. The eye feels comfortable. No surgery is advised."

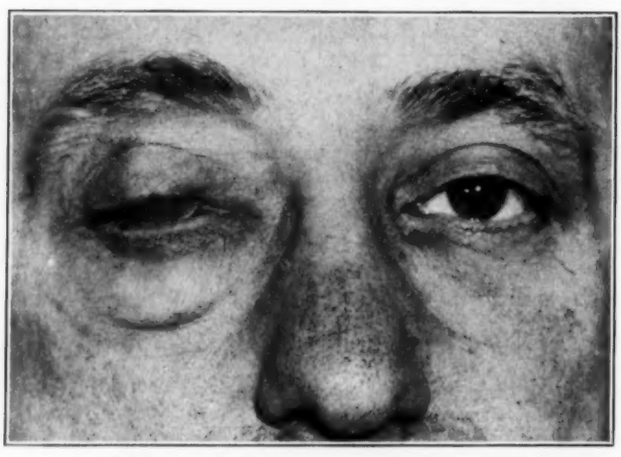

Fig. 2.—Right eye in April 1939 after treatment with sulfanilamide.

EXPERIMENTAL WORK

Nov. 21, 1938, the conjunctival surfaces of the right eye were thoroughly irrigated with a buffered salt solution and the washings filtered through a Berkefeld V candle. Part of the filtrate was prepared as a Frei antigen. This gave no reaction on intradermal tests in three cases of lymphogranuloma (A in the table) as well as in control cases. Five drops of the unheated filtrate were inoculated into three tissue cultures made up of embryonic guinea pig brain, fetal serum and buffered salt solution. A similar inoculum was put into cultures made up of embryonic guinea pig brain in buffered salt solution.[9] Control cultures consisted of an identical preparation without inoculum. At the same time at which the cultures were inoculated, three mice were injected intracerebrally with 0.3 cc. of the unfiltered washings and three mice with 0.3 cc. of the filtrate. These animals, observed subsequently for six weeks, showed no symptoms.

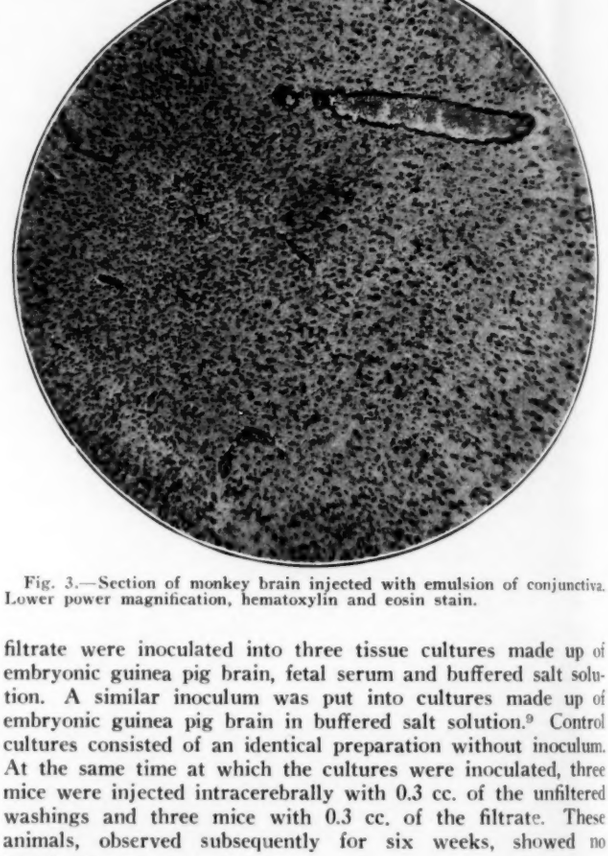

Fig. 3.—Section of monkey brain injected with emulsion of conjunctiva. Lower power magnification, hematoxylin and eosin stain.

Eight days after the cultures were inoculated the fluid portion was tested for sterility. At the same time 0.5 cc. was inoculated into fresh tissue cultures and 0.05 cc. was injected into each of six mice (intracerebrally). A portion of the fluid was also made up as antigen in the usual manner. Intradermal tests with this antigen gave positive results in four cases of venereal lymphogranuloma and negative results in two control cases. (B in the table). Fluid from the control cultures, on the other hand, gave no reactions (C in the table).

The results of the subcultures were negative, i. e. there was no indication of the presence of virus by mouse inoculation or by preparations of antigens from the cultures.[10]

Five days after inoculation two of the mice showed symptoms suggestive of a lymphogranulomatous infection: rough coat, humped back, emaciated appearance and ataxia. These animals were killed seven days after inoculation and from a 1:10 emulsion of the two brains antigen was made after part of the unheated emulsion had been passed to six mice. Of these, three showed the symptoms previously noted. This mouse brain antigen produced a positive cutaneous reaction in a known case of venereal lymphogranuloma (D in the table). We succeeded in transmitting the symptom-producing factor through passage in six mice.

9. A detailed account of the methods and preparations used here may be found in a recent study of the virus of lymphogranuloma in tissue cultures made by one of us (Sanders, Murray: J. Exper. Med. 1:113 [Jan.] 1940).

10. It is quite possible that the virus might have been transmitted serially in cultures if, instead of passing the fluid, an emulsion of the tissue and the fluid had been used as transfer inoculum. This fact was later established in other experiments with virus of lymphogranuloma in tissue cultures (M. S.).

A Macacus rhesus monkey was injected in the right parietal area with 1 cc. of an emulsion made by grinding up a small portion of excised conjunctiva of the patient with 2 cc. of Simm's solution. It is interesting to note that a portion of the same emulsion when used as an antigen gave positive reactions in cases of venereal lymphogranuloma and a negative reaction in a control case (E in the table).

Twenty days after inoculation a rise in temperature (to 103.4 F.) was noted, associated with transient weakness and tremors of the limbs contralateral to the site of injection.

On January 16, seven days after the onset of symptoms and twenty-seven days after inoculation, the animal was killed. Grossly, except for a moderate hyperemia, the brain showed little variation from the normal. Microscopic studies of various portions of the brain revealed a mild inflammatory reaction about the blood vessels with some degenerative changes (figs. 3 and 4) in the lower layers of the cortex on the right side. Microscopic examination of the spinal cord and of abdominal and thoracic viscera revealed no abnormal changes.

COMMENT

Repeated positive Frei reactions with reliable human antigen leave no doubt that the patient had at one time been infected with the virus of venereal lymphogranuloma. Moreover, the febrile response to the first intravenous injections of Frei antigen was typical of a patient infected with venereal lymphogranuloma (Hellerstroem,[11] Decker, Cañizares and Reider[12]). The serum protein values in this case were normal.

With regard to the site of inoculation, there was no history and no evidence (scars) that the virus had entered the body through the genitals. The anal fistula may have been nonspecific, since in the later course nothing in the rectum (absence of stricture or ulceration) suggested lymphogranuloma of the rectum.

The conjunctivitis of the right eye, however, followed the typical course of an infection with the virus of venereal lymphogranuloma. The infection spread to the lymph vessels and the regional lymph nodes and was in later stages of the disease characterized by chronic edema. As in the case reported by Levaditi, Bollack, Basch and Desvignes,[2] there was no pain associated with the optic process.

Fig. 4.—Section of monkey brain injected with emulsion of conjunctiva. High power magnification, hematoxylin and eosin stain.

Syphilis, tularemia and tuberculosis as etiologic factors of the ocular disease were ruled out. Leptothrix was not seen at biopsy.

Therapy with intravenous Frei antigen was not carried very far. Its failure is not surprising in view of the poor results in cases of late venereal lymphogranuloma of the genitals (esthiomene, ulcerations) in which stasis and edema are far advanced.

Sulfanilamide, however, terminated the activity of the process of the eye. Its efficacy in this case points to the infectious nature of the lesion. Besides, sulfanilamide, although to a lesser degree than sodium sulfanilate,[13] seems to be valuable especially in the later stages of venereal lymphogranuloma.

It is interesting to note that by intradermal tests on patients the virus was demonstrated in an extract of the tissue but not in washings from the eye. The virus was demonstrated, however, in cultures made from these washings. It seems probable that this intracellular virus was present in the washings in quantities too small to produce a positive Frei reaction without preliminary enrichment in culture.

SUMMARY

A third case of chronic unilateral conjunctivitis of seven years' duration due to the virus of venereal lymphogranuloma was observed. Treatment with sulfanilamide was effective in stopping the active process and in reducing the accompanying edema and stasis. Vision of the eye, however, had already been destroyed several years before. Demonstration of the virus by tissue cultures suggests that this technic may be a more delicate means of demonstrating the presence of the virus than animal inoculation.

35 East Eighty-Fourth Street—630 West 168th Street.

CORONARY THROMBOSIS OCCURRING IN A PILOT WHILE IN FLIGHT IN A SINGLE SEAT AIRCRAFT

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RANDOLPH FIELD, TEXAS

The prevention of any medical incident sufficient to incapacitate an individual while in flight is the primary duty of every physician charged with the care of fliers.

Although this medical incident may occur in any form, such as grand or petit mal, fainting from any cause, decreased judgment, perception and reaction time from any other illness or anoxemia, it is unusual to diagnose the precipitating cause, owing to the finality of the resultant crash.

In prevention, unfortunately, the inability to prognosticate in most cases the individual who will develop such an incident as a coronary infarct is well recognized. This difficulty in the Army Air Corps is mainly overcome by limiting older pilots to flying duties of a less fatiguing nature than actual combat flying and by placing them in multiplaced ships as command pilots with other pilots at the controls. Semiannual physical examinations, with electrocardiograms and teleoroentgenograms once a year also aid in relieving from flying duties those individuals with obvious defects.

However, in addition to the older pilot, the rapidly growing literature of coronary occlusion, now being more frequently diagnosed in the third and fourth decades, must also direct our attention to the possibility of this lesion in the younger pilot. It is believed that the case described here demonstrates the advisability of electrocardiographic studies in the annual examination of pilots of all age groups, instead of limitation as now done to those over 45 years of age. These studies would not only indicate the rare occasion when some pathologic condition might be suggested for further investigation, but also accumulate data in a controlled group which would prove of inestimable value for study and correlation in later years.

This case of coronary occlusion occurring in flight, in a single seat pursuit ship (type P-36), is reported because of its unusual form and its occurrence in an apparently healthy man of 27 in whose case another crash, "cause undetermined," might have been added to that list already too full. One similar case of coronary occlusion while in flight in a 35 year old pilot was reported by Benson.[1]

REPORT OF CASE

History.—The pilot, a second lieutenant, Air Corps Reserve, aged 27, had been on active duty with the Air Corps from March 30, 1939, to the date of his death, May 23, 1939. He had

11. Hellerstroem, J.: Bull. soc. franç. de dermat. et syph. **38:** 588 (April) 1931.
12. Decker, D. A.: Cañizares, Orlando, and Reider, R. F.: Mouse Brain Antigen, Arch. Dermat. & Syph. **40:** 397 (Sept.) 1939.
13. Hebb, Arthur; Sullivan, S. G., and Felton, L. D.: Pub. Health Rep. **54:** 1750 (Sept. 29) 1939.
1. Benson, Otis O.: Coronary Artery Disease; Report of Fatal Cardiac Attack in a Pilot While Flying, J. Aviation Med. **18:** 81 (June) 1937.

originally entered the Air Corps as a flying cadet July 1, 1932, and remained on active duty until Feb. 6, 1935. All previous physical examinations and the medical history obtained were essentially negative. From the period February 1935 to his entrance again on active duty in March 1939, I had examined this officer at six month intervals to fulfil the requirements of the semiannual examination of the Air Corps, with no abnormalities of the cardiovascular system being noted. No electrocardiograms were made. As a whole, he was considered one of the better physical specimens in a group of 200 highly selected and physically fit individuals.

On the day of his death, through history obtained from fellow officers, he awakened feeling perfectly well, ate a normal breakfast, and departed on a routine flying mission at 8:30 a. m. in a single seat pursuit ship. This mission did not necessitate altitudes in excess of 5,000 feet, but whether he may have flown to a higher altitude on his own initiative is not known. However, as he was a capable officer and obeyed orders, the latter event is not considered likely. On landing and climbing out of his ship at 9:30 he complained to a fellow officer that he was sick with epigastric distress and appeared cyanotic, weak and profusely perspiring. He was taken to his quarters in this fellow officer's car and walked to his room without aid at approximately 10 o'clock. No medical officer was informed of his condition until 12:30 p. m., at which time a visitor entering his quarters found him lying on his bunk, dead.

Additional history obtained after a search of his effects revealed that for approximately two months previous to his death, and from a time antedating his entry to active duty, he had been taking sulfanilamide prescribed by civilian physicians. This information had been withheld from the Army medical officers.

Autopsy.—This grossly demonstrated essentially the following: The weight of the heart was approximately 300 Gm., with a few petechial hemorrhages in the epicardium covering the posterior surface of the left ventricle. No valvular lesion was present. There was a slight amount of atherosclerosis in the arch of the aorta and considerable arteriosclerosis of the coronary system, with no gross evidence of roughening or superficial ulceration of any atheromatous plaque.

Other changes were found in congestion of the meninges and the brain with a slight amount of subarachnoid hemorrhage, congestion of the lungs, myocardium, spleen, liver, kidneys, pancreas, adrenals and genito-urinary tract, as well as a slight chronic adhesive pleuritis. The marked hemoconcentration was considered evidence of shock.

Microscopic Examination.—This was reported as follows: "Sections of the heart show ischemic infarction of the myocardium with round cell infiltration and the remains of some pigment. These foci without other evidence are quite suggestive of coronary artery disease. One of the forwarded sections shows a thrombus in a branch of coronary artery within the myocardium, although distinct ischemic changes are not present in the myocardium in this section. The thrombosis is recent and the material in some places is still adherent to the intima. The chronic passive congestion of the lungs is also in line with the left-sided cardiac changes. The small perivascular hemorrhages in the brain are generally regarded as secondary to anoxemia, usually terminal. It would seem that the cause of the sudden death is adequately explained by coronary occlusion by thrombosis."

COMMENT

The summation of evidence in this case points to arteriosclerosis of the coronary arteries with coronary occlusion by thrombosis, and probable insufficient time for gross alterations to become evident in the myocardium. As this cause was not definitely determined by the pathologist until after microscopic examination, any gross evidence of ulceration of an atheromatous plaque may have been so insignificant as to have been overlooked at the time of autopsy.

There appears to be no doubt that the terminal event took place in the air in the flight described. The possibility that the use of sulfanilamide was a contributing factor, with the formation of methemoglobin in the production of an anoxemia precipitating this event, is also present. Studies on the effect of anoxia on the cardiovascular system undertaken at the School of Aviation Medicine, Randolph Field, Texas, have revealed significant changes in the electrocardiogram at altitudes as low as 5,000 feet in normal persons. The latter would also add credence to the theory of anoxemia while in flight as a causative factor in this case.

School of Aviation Medicine.

OCCUPATIONAL DERMATITIS FROM HANDLING RESIN-LINED TIN CANS

LOUIS SCHWARTZ, M.D., WASHINGTON, D. C., AND
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Medical Director, U. S. Public Health Service, and Chief, Industrial Hygiene Service, State of California Department of Public Health, Respectively

In the course of the study of hazards to the skin in the canning industry of California we came across a number of cases of dermatitis diagnosed by the local physicians as "can poisoning." We were puzzled by the term, not knowing whether it meant that the workers were affected with dermatitis from the contents of the can or from some other substance with which they came in contact during the process of filling the cans. It never occurred to us that the condition might come from new, unused tin cans. However, while making studies in a number of canneries, we found that the workers engaged in

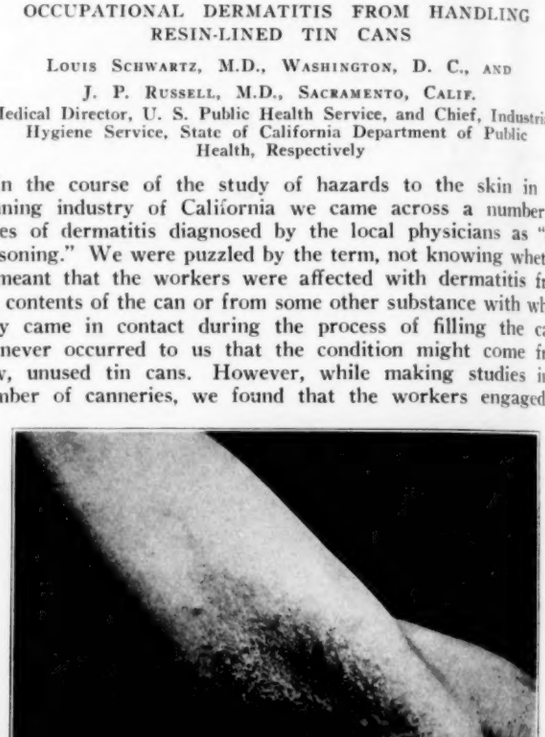


Fig. 1.—Dermatitis of axilla caused by dust from new resin-coated tin cans.

removing the new, unused tin cans from the freight cars and storing them in large storage rooms and then again removing them from the storage rooms to the traveling belts from which they are filled suffered from a dermatitis located principally in the cubital spaces and axillae. They claimed that this dermatitis was caused by dust coming out of the new cans, which at first seemed highly improbable, but actual investigations showed that such was the case. In the freight cars containing the cans and in the storage rooms in which they were stored there was a considerable quantity of metallic colored dust.

In one cannery three of the "forkers" were found to be affected (figs. 1 and 2). The forkers are the workers who move the tin cans from place to place by means of a contrivance called a fork, which consists of a handle across which at right angles there is a long piece of wood on which there are a number of forklike projections so spaced that each one fits into a can. By means of this a dozen or more cans can be lifted at one time. The three workers affected were patch tested with dust gathered from the traveling belt on which cans were placed. The dust was allowed to remain on the forearms for twenty-four hours and two of them showed a positive reaction.

Inquiries in other canneries elicited the fact that in some of them there had been cases of what they also called "can poisoning" at certain times among the forkers. It was found in other canneries examined that they had had no such cases.

Samples of the dust were obtained for chemical analysis from the cannery in which the three cases were seen. The dust was

found to consist principally of tin, iron and resin. The nature of the resin was that of a vinylite resin, but the exact composition of it could not be determined. Inquiry of the management of this cannery revealed the fact that about 10 per cent of the cans which they purchased were coated with a resin. Resin-lined cans were used for fruits and juices that might be discolored by contact with tin. Among such fruits are cherries and raspberries. Inquiries from a cannery where no such cases had occurred showed that they did not use any resin-lined cans.

Since the resin coating of cans is a comparatively recent process, and since no cases of dermatitis have been reported from tin or iron, it seems likely that this dermatitis was caused by sensitivity to the resin coating on the inside of the can, some of which flaked off in the form of dust.

An examination of the manufacturing process of these cans was made, but the actual composition of the resin coating was not disclosed by the manufacturer. The enamel or lacquer is applied to the clean tin plate as a thin film of the solution, after which the plate is passed through baking ovens wherein the volatile substances are completely evaporated from this film and the solid material polymerized or oxidized, thereby converting it into a hard, insoluble, highly chemical-resistant film of resin.

From the research department of the company manufacturing such cans the information was obtained that "the liquid enamel or lacquer which is applied to the tin plate is of a complex nature, consisting of a mixture of plasticizers and resins heavily bodied and reacted by heating. This is then thinned to the desired consistency and total solid content, for proper application, by means of a nontoxic petroleum solvent, similar in nature to that used in the varnish industry. Quite generally a lead-free drier is incorporated in the liquid enamel so as to facilitate the oxidation and polymerization of the film in the baking ovens. In general, the enamel is baked on the tin plate at a temperature of around 400 F. for a period of approximately 20 minutes. The finished enamel film weighs approximately 4/5 milligrams per square inch of tin plate. The finished film is different in all its physical and chemical characteristics from the liquid enamel film as applied to the tin plate."

In a personal interview with some of the chemists of a company manufacturing resin-lined cans it was learned that in addition to vinylite resin, which is used, there are certain plasticizers and driers the nature of which was not revealed.

Fig. 2.—Dermatitis of cubital space caused by dust from new resin-coated tin cans.

It was impossible to return to California and apply the different ingredients that go to make up vinylite resin lacquers to the skin of the three workers seen in the cannery. Therefore, it can be stated only that these workers were sensitive to the finished lacquer. The finished lacquer, however, may contain the polymerized resin, the plasticizer (which may consist of such chemicals as tung oil or China wood oil, or dibutylphthalate, or tricresyl phosphate), and a drier in the form of an inorganic salt of a resin, and fatty acids. Judging from our past experience, it is most likely that the sensitizer in the lacquer is one of the plasticizers. It may be possible, however, that in the baking process a decomposition of the resin takes place, because it is well known that vinylite resin, when coated over zinc, tin or iron surfaces and subjected to a temperature of 350 F. for a period of twenty minutes or more, shows a discoloration. Such a chemical reaction may result in the formation of zinc chloride or tin chloride, both of which are known to be skin irritants. That it is a sensitization dermatitis is shown by the fact that these workers all give a history of having worked for a considerable time before they were affected. That it is caused by sensitivity to the lacquer in the dust is shown not only by the patch tests but by the history that when workers who were affected were removed from their work as forkers to another part of the plant the condition cleared up. Similar cases occurred only in canneries where lacquered cans were used, and such "can poisoning" has occurred only since resin-lined cans have been used.

We were unable to find the exact chemical causing the dermatitis because we could not obtain full cooperation from the companies making the cans as to the exact composition of the lacquer and because we were unable to get the affected workers for more patch testing, owing to the distant location of the factories and the seasonal type of the work.

We are reporting these cases because it is the first time that such cases have been reported and because we feel certain that it was the resin coating of the tin cans that caused the dermatitis.

FAMILIAL EOSINOPHILIA

REPORT OF A CASE WITH BIOPSY OF LIVER

R. C. ATMAR, M.D., SAN ANTONIO, TEXAS

The term familial eosinophilia implies the presence of an increase in mature eosinophilic leukocytes in the blood of several members of a family in whom none of the known causes of eosinophilia, such as allergic states, dermatoses and parasitic infestations, are found. In 1911 Klinkert called attention to this condition and reported a family of six with eosinophil counts ranging from 7 to 15 per cent; three of the children, however, exhibited allergic manifestations. In 1930 Armand-Delille, Hurst and Sorapure [1] reported a family in which a boy of 8 had an eosinophil count of between 51 and 62 per cent with a leukocyte count that at times reached 29,000. Three sisters and one brother had eosinophil counts of 14, 27, 27 and 21 per cent, while the father had one of 7 per cent. Two other children had normal blood counts. In 1933 Sloan Stewart [2] reported four families in each of which several members exhibited a distinct, persisting and unexplained eosinophilia. There are many cases reported in which there are high eosinophil counts associated with a high leukocytosis, but in searching through the literature I could find only five families on record who showed a persistent unexplainable eosinophilia in several members of the family.

REPORT OF CASE

A Mexican woman aged 25, admitted to the charity clinic of Robert B. Green Hospital on Aug. 22, 1938, complained chiefly of sacral backache, which had begun soon after the birth of a child three months previously. The sacral backache was accompanied by a sense of pelvic heaviness and slight leukorrhea.

The patient was thin and somewhat anemic looking but did not appear acutely ill. The skin was smooth and normal in appearance. No areas of pigmentation were seen. There was no enlargement of the thyroid gland or lymph nodes. The head, neck, heart and lungs were essentially normal. Inspection of the abdomen revealed an umbilical hernia of moderate size. The blood pressure was 130 systolic and 90 diastolic, the pulse rate 80, the temperature 98 F. and the respiratory rate 24.

Pelvic examination showed an acquired retrodisplacement of the uterus and a third degree retroversion.

Laboratory examination gave the following results: There were 4,190,000 red blood cells, with a hemoglobin content of 80 per cent, and 27,100 white blood cells. The differential count revealed 16 per cent neutrophils, 24 per cent lymphocytes, 58 per cent eosinophils and 2 per cent basophils. Two days later the total white cell count was 30,000, with 70 per cent eosinophils. All the eosinophils were of the mature variety. The Wassermann and Kahn tests of the blood gave negative reactions. Urinalysis showed nothing abnormal. Repeated examinations of feces for intestinal parasites or ova gave negative

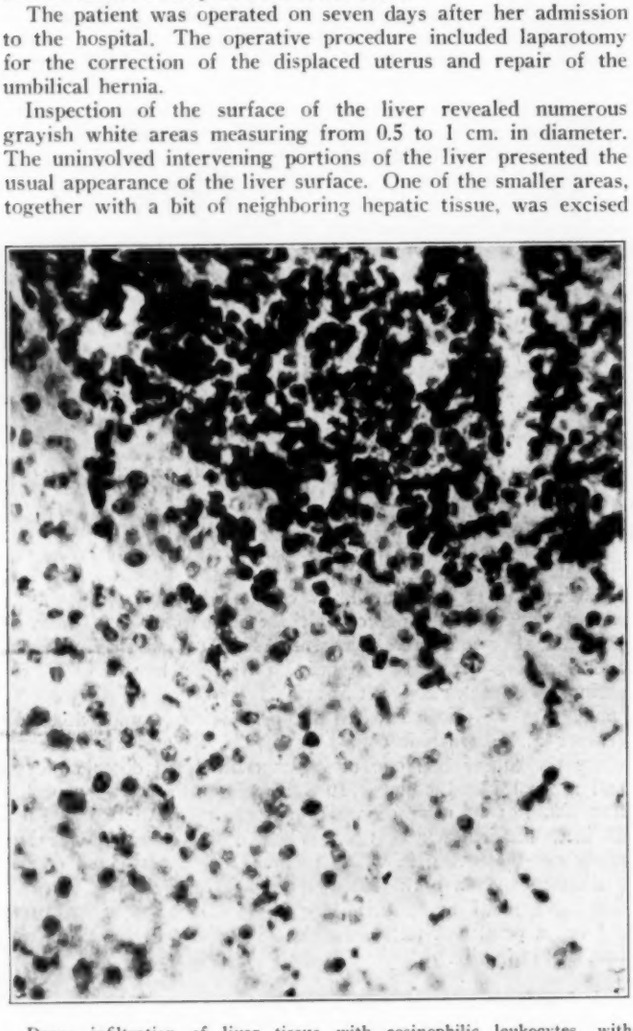
1. Armand-Delille, P. F.; Hurst, A. F., and Sorapure, V. E.: Familial Eosinophilia, Guy's Hosp. Rep. **80**: 248 (April) 1930.
2. Stewart, S. G.: Familial Eosinophilia, Am. J. M. Sc. **185**: 21 (Jan.) 1933.

results. An excess of neutral fats was found. The basal metabolic rate was plus 30. A study of the chemical changes of the blood gave the following results: nonprotein nitrogen 27.6 mg. per hundred cubic centimeters, creatinine 1.1 mg., sugar 79 mg. The icterus index was in units.

An x-ray study of the lungs showed considerable cloudiness and increased density in both lower lobes.

The patient was operated on seven days after her admission to the hospital. The operative procedure included laparotomy for the correction of the displaced uterus and repair of the umbilical hernia.

Inspection of the surface of the liver revealed numerous grayish white areas measuring from 0.5 to 1 cm. in diameter. The uninvolved intervening portions of the liver presented the usual appearance of the liver surface. One of the smaller areas, together with a bit of neighboring hepatic tissue, was excised



Dense infiltration of liver tissue with eosinophilic leukocytes, with complete replacement of hepatic cells in the center of the area.

for microscopic study. The sections showed dense infiltration of the liver tissue with eosinophilic leukocytes which resulted in complete replacement of hepatic cells in the center area, as shown in the illustration. Neighboring liver cells appeared normal.

Results of Subsequent Blood Examinations

Date	White Cells	Eosinophils, Per Cent
Sept. 3, 1938	10,800	24
September 7	19,700	53
September 11	16,450	58
October 4	42,700	81
December 15	20,100	59
June 28, 1939	10,650	34
Jan. 21, 1940	8,800	29

The postoperative period was uneventful. There has been a gain in weight of 20 pounds (9 Kg.) and the patient has enjoyed excellent health.

Subsequent examinations of the patient's blood gave the results tabulated.

The patient has two brothers and two sisters, all of whom, with the exception of one of the sisters, showed eosinophilia. A brother aged 11 years had a total white cell count of 7,550, with 16 per cent of eosinophils, while the other brother, who is 8 years old, was found to have a total white cell count of 6,350, of which 15 per cent were eosinophils. The 5 year old sister had 6,000 leukocytes with a differential count showing 20 per cent eosinophils.

The patient's two children, a girl aged 4½ years and a boy aged 19 months, both showed an eosinophil count well above the normal limit, with total white cell counts of 12,400 and 10,300; the percentage of eosinophils was 31 and 13 respectively.

Blood examinations made on the patient's father, mother and husband showed nothing abnormal.

All members of the patient's family, and particularly those with eosinophilia, were carefully studied for evidence of the known causes of eosinophilia, with negative results.

COMMENT

This case is being reported because of the interesting gross and microscopic condition found in the liver, an addition, so far as could be determined, to previously reported cases of unexplained eosinophilia. It represents an unusual blood picture and presents difficulties in diagnosis, and the fact that the patient is one of four in a family of five children with eosinophilia and that her own children show a similar blood picture would seem to argue quite definitely in favor of a diagnosis of the familial type of eosinophilia rather than of eosinophilic leukemia as the explanation of the hematologic condition.

The elevated basal metabolic rate and infiltration of tissues with eosinophils are conditions recorded by Bass [3] as occurring in eosinophilic leukemia. On the other hand, while it is true that in this case the eosinophils are of the mature variety, it is a noteworthy fact that there has not been a persistent increased white count.

205 Camden Street.

Therapeutics

THE THERAPY OF THE COOK COUNTY HOSPITAL

EDITED BY BERNARD FANTUS, M.D.
CHICAGO

NOTE.—*In their elaboration, these articles were submitted to the members of the attending staff of the Cook County Hospital by the director of therapeutics, the late Dr. Bernard Fantus. The views expressed by various members are incorporated in the final draft for publication. When completed, the series will be published in book form.*—ED.

THE THERAPY OF SUBVITAMINOSIS B_1

IN COLLABORATION WITH DRS. EUGENE F. TRAUT AND REGINA STOLZ GREENEBAUM

Subvitaminosis B_1, beriberi and thiamine deficiency are synonymous terms. "Dry beriberi," a peripheral neuropathy produced by vitamin B_1 deficiency, occurs in all economic classes in Chicago. It is especially common at Cook County Hospital because of the poverty of its patients. "Wet beriberi," characterized by peripheral neuropathy and edema, is much less common. It may be overlooked because in this form the peripheral neuropathy "is so often only mild or minimal." [1] Since the term "beriberi" is associated by many with "wet beriberi" of the Orient, the term "subvitaminosis B_1" seems preferable for the condition as we commonly see it.

3. Bass, M. H.: Eosinophilic Leukemia, Am. J. Dis. Child. 41: 1394 (June) 1931.

Dr. Fantus died April 14, 1940.

Dr. Norman Jolliffe, of New York, gave the authors important suggestions on this work.

Much of the information contained in this article was obtained from the series by the Council on Pharmacy and Chemistry and the Council on Foods, published in THE JOURNAL, Feb. 19, 1938, page 577, and subsequent issues, and from R. R. Williams and T. D. Spies "Vitamin B_1 and Its Use in Medicine," New York, Macmillan Company, 1938.

1. Jolliffe, Norman: Personal communication to the authors.

Crystalline vitamin B_1 hydrochloride has been named thiamin chloride or, preferably, "thiamine hydrochloride."

DIAGNOSIS

In the successful use of vitamins, as in all other therapy, correct diagnosis is essential. Vitamins are specifics for diseases produced by their lack. They are valueless, though usually harmless, unless a deficiency of them is present. Each vitamin is specific in the treatment of the symptoms resulting from a deficiency of it. It is not helpful in the amelioration of symptoms produced by a lack of other vitamins, although the conditions favoring an insufficiency of one frequently produce a lack of others.

CONDITIONS IN WHICH SUBVITAMINOSIS B_1 MUST BE SUSPECTED

Any patient may have a thiamine deficiency. The usual diet of refined foods deprives one of some of the richest sources of this vitamin and at the same time increases one's need for it. The body requirements for vitamin B_1 are thought to be proportional to the metabolic rate and the non-fat calorigenic (including alcohol) intake. A person who refrains from all food needs little vitamin B_1. A diet high in refined carbohydrates increases the need for thiamine. No food contains a large amount of vitamin B_1 comparable to the vitamin C content of orange juice. For example, an orange which furnishes 90 cc. of juice yields 45 mg. of ascorbic acid, nearly the daily human requirement. On the other hand, 3 ounces (90 Gm.) of liver or pork muscle or 1 ounce (30 Gm.) of shelled peanuts provides only from 16 to 25 per cent of the calculated thiamine needed daily by the average person. Much of what is contained in raw foods is destroyed by the heat of cooking or may be discarded in the water of boiling. The intake of vitamin B_1 of even the well-to-do probably allows little if any margin of safety. Any slight increase in need such as occurs with violent exercise or a mild infection may suffice to produce subvitaminosis B_1.

Thiamine deficiency must be suspected under the following circumstances:

1. Inadequate intake of foods containing vitamin B_1:

(*a*) In a charity hospital, poverty is perhaps the most frequent cause of an inadequate diet. The diet of the poor is likely to be rich in cheap refined sugars and starches almost devoid of thiamine but deficient in liver, eggs, whole grain cereals and nuts richer in thiamine but comparatively expensive.

(*b*) Ignorance of the essentials of an adequate diet is a very important cause of inadequate ingestion of vitamin B_1. Food faddists may suffer for this reason.

(*c*) Diets used in therapy, if continued for a long time, frequently contribute to this deficiency. Diabetic patients with their disturbed carbohydrate metabolism seem to need more of this substance. Poorly planned antiobesity diets are also likely to be deficient in vitamin B_1 as well as in the fat soluble vitamins A and D. It is worth observing that in spite of being low in absolute amounts of vitamin B_1 the vitamin calory ratio is usually better in well planned reducing diets than in prescribed high calory, vitamin-rich diets, and certainly the ratio is better than in the average American diet. Smooth diets for patients with colitis reduce uncooked food to a minimum, thus eliminating other important sources of vitamin B_1 such as whole grains.

(*d*) Chronic alcoholism is the most frequent predisposing factor in cases of severe involvement at the Cook County Hospital. Alcohol provides non-fat calories which increase the need for thiamine. "Alcoholic neuritis" has been definitely shown to be a manifestation of thiamine deficiency. Loss of appetite often follows a long spree. The chronic alcoholic addict with limited funds buys liquor rather than food. Absorption is impaired by the effects of alcohol on the gastrointestinal tract. In cases of "alcoholic cirrhosis" of the liver, utilization is also impaired. Thus the chronic alcoholic addict has increased need, diminished intake, faulty absorption and possibly impaired utilization.

(*e*) Absence of teeth, with resulting inability to chew foods containing thiamine, may be a predisposing factor.

(*f*) The intravenous administration of dextrose to a patient whose thiamine stores are depleted may precipitate clinical subvitaminosis B_1.

2. Inadequate absorption. (*a*) Persistent vomiting produced by esophageal or pyloric stenosis, hyperemesis gravidarum, chronic intestinal obstruction or any other cause may result in subvitaminosis B_1.

(*b*) Chronic diarrhea, regardless of etiology, interferes markedly with absorption. The cathartic habit may also prevent adequate absorption.

(*c*) Short circuiting of the bowel may deprive the patient of a large amount of absorptive surface.

(*d*) Achlorhydria and achylia are sometimes associated with vitamin B_1 deficiency. Whether this relation is accidental or etiologic is unknown.

3. Increased need. (*a*) Infection, especially if of long duration and associated with fever, predisposes to subvitaminosis B_1 by increasing the metabolic rate and diminishing appetite. Typhoid and tuberculosis are examples.

(*b*) Thyrotoxicosis is another predisposing factor.

(*c*) In pregnancy and lactation the needs of both the mother and the rapidly growing fetus or infant must be met. The pregnant or lactating woman probably needs about five times as much thiamine as a nonpregnant adult.

(*d*) Violent exercise increases the thiamine requirements by increasing the metabolic rate.

4. Disturbed utilization. (*a*) Liver disease in some way affects the ability of the body to store or utilize vitamin B_1 and therefore larger amounts of it must be supplied.

(*b*) Persons with diabetes mellitus seem to have an increased need for thiamine. Vitamin B_1 plays an essential part in intermediate carbohydrate metabolism, which is disturbed in this disease.

5. Disturbed distribution.

Arteriosclerosis interferes with the distribution of vitamin B_1 to the tissues. An intake adequate for young adults may be insufficient for the aged.

SYMPTOMS AND SIGNS OF EARLY SUBVITAMINOSIS B_1

The earliest symptoms of early subvitaminosis B_1 are usually those of a peripheral neuropathy. The pathologic change is degenerative rather than inflammatory; hence the condition is a neuropathy rather than a neuritis. The common complaints are paresthesias such as numbness, burning or tingling, lack of endurance in walking or cramps in the leg muscles. The nervous symptoms and manifestations are usually but not always first noticed in the lower extremities. They are frequently bilateral and symmetrical. The vibratory sense is diminished or lost. Ankle jerks may disappear. A difference in the intensity of the painful sensation produced by pricking the patient on a normal part of the

body contrasted with what he feels on an abnormal part is useful as a test in early subvitaminosis B_1.

Mild cardiovascular involvement shows itself as dyspnea on exertion, palpitation, fatigue and rapid pulse.

Diminished appetite with loss of weight may precede or accompany the other symptoms.

MODERATELY ADVANCED SUBVITAMINOSIS B_1

At any stage the patient may complain of pain along a nerve trunk, even along the intercostal nerves. The muscular weakness may lead to drop foot. Atrophy of the affected muscles develops. It involves the thigh with the progress of the disease. The knee jerks decrease or disappear. The upper extremities may then be affected in similar fashion beginning at the distal portions and extending toward the trunk. As the sensory changes advance, pain and numbness increase. The hypesthesia or anesthesia usually assumes a stocking or glove pattern.

Dyspnea is noticed on slight effort. The heart enlarges symmetrically or predominantly to the right or to the left. Peripheral vasodilatation may show itself as a pinkness of the hands and feet. When the blood pressure is taken the sounds over the brachial artery may be long and booming. The common electrocardiographic changes are inversion of the T wave in any lead and low amplitude and prolongation of the QRS. Diminution of bowel tone and of peristalsis results in constipation. Diarrhea may alternate with or replace constipation.

ADVANCED SUBVITAMINOSIS B_1

The muscular and sensory changes increase. They may involve the trunk. The patient then becomes bedridden. Contractures may develop. The only cranial nerves likely to be affected are the vagus and the abducens. Vagus involvement produces vocal cord paresis and possibly tachycardia. The oculomotor nerves, especially the abducens, may be affected in cases of Wernicke's syndrome, now recognized as a manifestation of subvitaminosis B_1.

As cardiovascular failure increases, breathlessness is accompanied by the accumulation of edema. Hypoproteinemia, frequently a concomitant effect of a diet low in vitamin B_1, contributes to the production of the edema. Subvitaminosis B_1 and hyperthyroidism produce the only types of heart failure marked by an increased velocity of the blood, resulting in a decreased circulation time.

Advanced emaciation may be masked by the increased retention of water in cases of wet beriberi.

NEUROPATHIES LESS GENERALLY ACCEPTED AS DUE TO SUBVITAMINOSIS B_1

"Diabetic neuritis" is now more generally recognized as resulting from thiamine deficiency. Postinfectious or toxic neuritis, trigeminal neuralgia, some cases of sciatica and herpes zoster may be manifestations of B_1 deficiency or may be complicated by it.

DIAGNOSIS

The diagnosis of subvitaminosis B_1 must be based on symptoms and physical signs until a satisfactory chemical method for determining thiamine absorption and utilization can be found for clinical use. The therapeutic test is at present less expensive than chemical determinations. Subvitaminosis B_1 must be differentiated from neuropathies of other origin. It is the one neuropathy in which treatment is dramatically successful. A therapeutic test is therefore indicated whenever lack of vitamin B_1 is the suspected etiologic factor.

While thiamine is the most commonly deficient vitamin, especially among the poor, its expense precludes its use as a placebo in a charity hospital.

TREATMENT

Prophylaxis.—An adequate diet is the best prophylaxis for subvitaminosis B_1. Each history should include a detailed account of the patient's food habits. Particularly in a charity hospital, the amount, kind and frequency of ingestion of meat, eggs, fruit, vegetables, nuts, bread and cereals should make up a paragraph of the history. The manner and duration of cooking vegetables with particular attention to the disposal of the water or juice should be noted. In spite of a good diet, peculiarities in individual metabolism may produce subvitaminosis B_1. Almost every one must be dietetically reeducated. The poor must be supplied with the wherewithal for an adequate diet. The daily requirement of vitamin B_1 varies. The average adult is believed to need from 1 to 1.5 mg., or from 300 to 450 international units, of thiamine hydrochloride daily, depending on his non-fat calorigenic intake. This is equivalent to from 10 to 15 international units per hundred calories consumed, assuming that the average diet affords 3,000 calories. The preschool child is thought to require at least 20 to 25 international units per hundred calories and the pregnant or lactating woman about 50 international units per hundred calories. In pregnancy or the puerperium a diet yielding 3,000 calories would require 5 mg., or 1,500 international units, of thiamine hydrochloride daily. With the heightened metabolism of thyrotoxicosis the patient should have from 1,500 to 3,000 international units, or from 5 to 10 mg., each day. To obtain an adequate amount of thiamine an adult should have daily at least 1 pint (500 cc.) of milk, one or two eggs, at least one serving of meat, two servings of fruit (one raw), two servings of vegetables (one a legume), nuts and whole grain bread and cereals. For a balanced diet butter should be added. Nuts are the richest of any of the ordinary foods in this vitamin. Peanuts and peanut butter are within the reach of even the poorest. Roasting and processing affect their thiamine content only slightly. Liver is desirable because of its high content of thiamine and many other necessary food elements. Pork muscle is much richer than other meats in vitamin B_1. Peas and other legumes, wheat germ and brewers' yeast are important sources of thiamine. Much thiamine is dissolved in water during the boiling of foods. People must be taught to use this water in soup. Prolonged cooking destroys vitamin B_1. In contrast to the other factors in the B complex known to be essential for human beings, thiamine is heat labile. Raw beans, for instance, are exceptionally rich in this substance; baked beans are almost devoid of it. Consequently rapid cooking in a minimum of water and utilization of that water are desirable.

Since it is difficult to obtain an adequate amount of this vitamin in unrestricted diets, therapeutic diets prescribed for long periods must be carefully scrutinized to prevent thiamine lack. The prevention of "diabetic neuritis" makes this consideration especially important in planning diabetic diets. Diets for gastrointestinal disease are likely to be deficient. Cutting down on roughage eliminates much thiamine-containing substance. This difficulty can be avoided by prescribing sufficient milk and eggs and by sufficiently restricting the use of refined carbohydrates. Diets low in protein tend to be low in vitamin B_1. They should not be continued over long periods.

In diets restricted in thiamine-containing foods, it is advisable to supply this vitamin in yeast, wheat germ, vitamin B concentrates or as pure thiamine hydrochloride. The supply of other vitamins and minerals must also be considered. The amount of vitamin B_1 found in many commercial polyvitamin preparations is insufficient, in the recommended dosage, to supply the body's need if they are the sole source of this vitamin.

The Therapeutic Test.—The response to an adequate dose of thiamine hydrochloride administered parenterally is usually prompt in alleviating the symptoms of vitamin B_1 deficiency. Thiamine hydrochloride will not affect symptoms of other origin. Vitamin B_1 is most effective when administered parenterally. The parenteral route is imperative in a therapeutic test to insure absorption. Thiamine hydrochloride is injected subcutaneously at Cook County Hospital because of its more gradual utilization by that route. Intravenous injection results in more rapid excretion and requires an intern's attention. The subcutaneous is as effective as the intramuscular or intravenous route. Although much larger doses have been recommended in the literature, we have found that a subcutaneous injection of 10 mg. daily is usually adequate; 30 mg. daily may be needed in cases of severe involvement. We recommend employing this dose for ten days in a therapeutic test. The first signs of improvement are disappearance of edema, slowing of the pulse (if it has been rapid) and diminution of neuritic pain, of paresthesias and of tenderness in the calves. An increased feeling of well-being is especially characteristic in the cases of mild involvement. Recovery of motion and sensory perception are much slower. They will not occur within the period of the therapeutic test. Reflexes usually return and atrophy disappears some time after the restoration of motor power. Alleviation of any of the characteristic symptoms and signs is a confirmation of the diagnosis of B_1 subvitaminosis.

If no improvement occurs aften ten daily injections of 30 mg. of thiamine hydrochloride in the severe cases, and of 10 mg. in the majority of cases, curative effects are not to be expected. Another diagnosis should then be sought immediately. Thiamine treatment, itself innocuous, may be harmful by distracting the physician from a more thorough search for the true cause of the disability. We have seen a tumor of the spinal cord, syphilis of the central nervous system and nephrosis thus overlooked.

The Continuance of Treatment.—After the diagnosis of thiamine deficiency has been established by a favorable result of the therapeutic test, the underlying cause of the deficiency must be sought and, if possible, remedied. Injections of adequate amounts of thiamine hydrochloride must be continued until cure is effected. It is better to give too much than too little. This holds especially for cases of cardiac disorders, in which penurious dispensing may result in death. Giving thiamine hydrochloride in sufficiently large doses is economical in saving hospital days. Cook County Hospital saves by buying crystalline thiamine hydrochloride and making its own solution. Failure of absorption is avoided by the parenteral method of administration.

In the light of present information we recommend a daily injection of 10 mg. for the first few weeks, except in cases of very severe involvement, in which 30 mg. may be used for two weeks. More widespread use of acceptable excretion tests may alter this advice. The administration of the vitamin should continue until complete recovery has occurred. After the deficiency is overcome, equilibrium should be maintained by an adequate supply in the food or by thiamine supplement if needed. The vitamin B_1 intake can be continued at the desired high level by supplying a diet containing wheat germ, yeast, rice polishings or their extract, liver, whole wheat bread and cereals, eggs, nuts, lean pork and legumes.

In addition to the parenteral administration of thiamine hydrochloride, a high intake of other necessary food elements is essential. When one vitamin deficiency exists, other food deficiencies are to be suspected. The components of the B complex are interrelated in the intracellular enzyme systems. With an adequate supply of all of them the patient will progress more rapidly than if some are missing. Since essential unknown dietary elements presumably exist, it is impossible to prevent all deficiencies with vitamin concentrates alone. Without clinical or laboratory evidence of a lack of other vitamins, it seems unnecessarily expensive to give other vitamin concentrates when the diet is adequate.

If a patient leaves the hospital before his cure is completed, the Visiting Nurses' Association of Chicago will continue his injections at home under a physician's supervision. Many hospital days may be saved by this service.

We caution against the intrathecal administration of thiamine. Convincing evidence that this is a safe method of administration is lacking. Its advantages over intravenous or subcutaneous injection have not been confirmed. Any of its reported good effects may be ascribed to the nonspecific benefit of an aseptic meningitis with the accompanying hyperemia of the meninges. We have had no experience with the massive doses prescribed by Naide [2] for the treatment of the ischemic pain in peripheral arterial disease.

The ultimate outcome of therapy and the rate of improvement depend on the duration and extent of damage. It is thought that the regeneration of nerves occurs at the rate of about 1 mm. a day. Months or even years may be required for complete regeneration of the nerves to the feet. In very severe cases of long duration with degeneration of the neurons in the anterior horns of the spinal cord or in the posterior ganglions, complete recovery may not occur.

ASSOCIATED CONDITIONS

Subvitaminosis B_1 and pellagra are frequently associated, especially in cases of chronic alcoholism. In such cases nicotinic acid should be administered in adequate doses in addition to thiamine hydrochloride. Riboflavin and vitamin B_6 deficiencies should also be sought, as should subclinical scurvy, subvitaminosis A and subvitaminosis D. In the presence of liver damage, subvitaminosis K may also occur. Achlorhydria and achylia are likewise frequent in cases of thiamine deficiency. Hyperchromic or hypochromic anemias are sometimes associated with a lack of the B vitamins. All these deficiencies should be appropriately treated if present.

Accessory therapy includes measures for the prevention of permanent deformities in paralyzed extremities. Moving all the joints passively through their full range of motion once a day prevents contractures. Holding the joints in one position in full casts encourages permanent stiffness and favors atrophy. Splints should be removable. Massage has been thought beneficial in improving the circulation of paralyzed muscles. Active exercise should be encouraged. Exercise should not

2. Naide, Meyer: The Use of Vitamin B_1 in Rest Pain of Ischemic Origin, Am. J. M. Sc. **197**: 766-773 (June) 1939.

be carried to the point of fatigue. We have seen no benefit from electrical stimulation.

Before discharge from the hospital the patient should understand the nature of his disease. He should be urged to continue to eat foods rich in thiamine and if necessary to continue the injections. Recurrences of thiamine deficiency are frequent.[3] One should observe the patient periodically with this in mind. In cases of recurrences, it may be necessary to provide some sort of thiamine supplement indefinitely.

Special Article

CONFERENCES ON THERAPY

MANAGEMENT OF DIABETIC EMERGENCIES:

I. GENERAL TREATMENT

NOTE.—*These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital, with the collaboration of other departments. The questions and discussions involve participation by members of the staff of the college and hospital, students and visitors. The next report will concern "Management of Diabetic Emergencies: II. Treatment of Surgical Patients and Children."*

DR. EUGENE F. DU BOIS: The management of the ordinary, uncomplicated case of diabetes is not difficult these days; the management of emergencies will always remain difficult. Dr. Tolstoi will take up the clinical aspects.

DR. EDWARD TOLSTOI: As the result of recent experiments performed in collaboration with Dr. Weber and Mr. Toscani, we have been led to adopt a somewhat less orthodox point of view in the treatment of the diabetic patient. We found that our experimental subjects were free from the symptoms of diabetes in spite of glycosuria when they were receiving a diet of 75 Gm. of protein, 60 Gm. of fat and 200 Gm. of carbohydrate, and protamine zinc insulin in daily doses of 50 units. Two rather unusual patients whom we observed in the metabolism ward for periods of fifty to sixty days maintained their weight. I want to emphasize this point. They also had no thirst or polyuria; they had no ketonuria, and they were in nitrogenous equilibrium in spite of the fact that they excreted as much as 150 Gm. of sugar some days, and in spite of the fact that there was an ever present postprandial hyperglycemia. From such experiments we postulated that for patients treated with protamine zinc insulin the guiding features of satisfactory treatment should be (1) the maintenance of weight, (2) freedom from symptoms and (3) absence of ketonuria. Furthermore, we were not concerned about the hyperglycemia or the amount of dextrose excreted. It is our belief that if the diabetic patient is made to utilize a quantity of carbohydrate essential for his particular metabolic needs the excess may be excreted without damaging results.

We have had further opportunity to pursue these studies in ambulatory cases in the outpatient department, and our results there have been gratifying. We paid little attention to the glycosuria; we were guided by the principles mentioned, and the majority of our patients have done exceedingly well. They have been liberated from multiple injections of insulin and now receive one injection of insulin a day, putting their syringes away for the remainder of the time as they would their toothbrushes.

DR. DU BOIS: Are you referring to insulin now or to protamine zinc insulin?

DR. TOLSTOI: All reference will be to protamine zinc insulin unless I specifically state otherwise.

Simultaneously there have been others in the same field who have adopted the point of view that the patient may excrete sugar with safety. The quantity of sugar excreted in twenty-four hours has been a question of controversy. Some say a diabetic patient is well controlled when he excretes only 10 Gm. of sugar in twenty-four hours. Others permit him to excrete as much as 40 Gm. of sugar a day. Our patients excreted as much as 150 Gm. on occasions. Both of the patients whom we studied recently at this hospital excreted 100 Gm. daily for thirty days, a total of more than 6 pounds (3 Kg.) of sugar. They were in nitrogenous equilibrium and they felt perfectly well.

As to diabetic emergencies, there are in reality only two which are directly and intimately associated with diabetes. One of these is acid intoxication, or ketosis, and the other, which involves the insulin treated diabetic patient only, is the hypoglycemic syndrome.

ACID INTOXICATION

The chief causes for ketosis, the more hazardous complication of the two diabetic emergencies, are either medical or surgical infections—a common cold, a boil, a sore throat or the more serious conditions such as pneumonia or an acute surgical state of the abdomen. All of these are potential causes of ketosis. Others are departure from dietary restrictions and eating too much, the omission of insulin, and hyperthyroidism. This year I have had an opportunity of seeing two patients in whom stubborn ketosis developed during severe sunburn. It is noteworthy that a simple condition such as pharyngitis may decompensate the diabetic patient so that it precipitates not only ketosis but coma as well.

We should differentiate between the two terms "ketosis" and "coma." The clinical differentiation is especially important. Coma is a state in which the patient is unable to respond to any and all stimuli. In ketosis he may be up and about. The distinction between coma and ketosis has been made by a laboratory test by Joslin and his school. They feel that if the carbon dioxide combining power is below 20 the patient is apt to be in coma; if it is above 20 he is not in coma.

Let us consider how trouble arises for the diabetic patient who contracts an infection. First he takes less food because he loses his appetite. He has been taught that in such a situation he should omit his insulin. Here the fault lies with the physician who fails to realize that even though the diabetic patient does not ingest any food he will draw on his own storehouse. These foods cannot be utilized properly without insulin. The result is that ketone bodies begin to form. The little endogenous insulin that he may have is rendered less potent by the infectious process, which thus furnishes another factor conducive to ketosis. As the ketone bodies begin to form, the patient shows a characteristic syndrome that sets in rather insidiously. At first he feels weak and listless. He is perfectly content to be left alone. A little later thirst develops, and frequency as well as polyuria. He may also complain of headache, backache and aches in the calves of both legs. These symp-

3. Vorhaus, M. G.: Evaluation of Vitamin B (Thiamin Chloride) in the Treatment of Polyneuritis, Am. J. M. Sc. **198**: 837-844 (Dec.) 1939.

toms are annoying, but they do not alarm the patient particularly until he begins to vomit. With the vomiting there is epigastric pain. This pain may further localize in the right lower quadrant. When the patient is seen at this time, the physician's attention is directed to the abdomen. An examination of the abdomen may show not only slight rigidity but even rebound tenderness. Appendicitis, of course, is the condition that suggests itself. At this point a blood count reveals leukocytosis with anywhere from 20,000 to 80,000 cells and a good percentage of immature neutrophils. Further examination of the patient will reveal that he is flushed; the tongue is parched, dry and beefy red, as is the throat; the eyeballs are soft; the skin is dry. The question arises: Is it uncomplicated ketosis or a surgical abdominal condition which has precipitated the ketosis?

Laboratory data at this point are of importance: in the blood sugar varying from 250 to 1,000 mg. per hundred cubic centimeters, low carbon dioxide combining power, elevated nonprotein nitrogen, hemoconcentration; in the urine large quantities of sugar, large quantities of acetone and diacetic acid. These establish the diagnosis. What are we going to do with a patient in this situation?

First, let us consider the one whose condition is not far advanced, the patient as we see him in the clinic. He may report a sore throat. Examination of the urine reveals a 4 plus acetone reaction and diacetic acid. The skin and the tongue are dry, there is dehydration and there are listlessness and the desire to be left alone. We tell the patient "Go home, take a tablet or two of table salt (1 Gm. of salt) every hour, and follow that with a glass of water; in addition, take all the hot salt broth you can." We teach him to examine his urine for acetone and tell him to do so every two hours, and as long as acetone is present to give himself insulin (regular soluble) after each urine examination until the acetone bodies disappear. The dosage of insulin is determined by the urine analyses for sugar. He is told to take 25 units if the result of the test is yellow or red, 15 units if the specimen is green, and the juice of an orange if the Benedict solution is unchanged after boiling. This simple rule also protects the patients against insulin overdosage. We have had such a patient come to see us on Friday and return on Monday weighing 8 pounds (3.6 Kg.) more and acetone free. Although the glycosuria was still present, she retained most of the fluid taken.

In the more advanced stages of ketosis the patient is admitted to the hospital and put to bed. Warm bags are applied to the extremities and he is wrapped in blankets. We cannot give this patient fluids by mouth because he is vomiting, so fluids are introduced by clysis. What kind of fluids? Dextrose solution, and since the patient is losing salt while losing water we give a saline solution of dextrose. It is well to start with 1,000 cc. of 5 per cent dextrose in saline solution. How much insulin? That varies; anywhere from 25 to 50 units. All agree that an amount above 50 units is unnecessary. Perhaps even smaller doses at frequent intervals are more effective than a single large dose. We have given 35 units at the start. The urine specimen is examined every hour or hour and a half for acetone bodies, and the administration of soluble insulin is continued until the ketone bodies vanish. As soon as the ketone bodies begin to disappear, the patient's flush vanishes, the tongue becomes moist, the cheeks fill out a bit and he is able to take some fluids by mouth. Salty broth is continued, also milk and orange juice are given, and the urine is reexamined frequently. The administration of insulin is continued for a day or two after the ketone bodies have disappeared.

How much insulin should be given after the ketone bodies have disappeared? We use the simple guide just mentioned: If the urine specimen is yellow by the Benedict test we give 25 units; if it is green, 15 units. If it is blue we give only orange juice. After a two day period the patient will be able to take food by mouth, and he can then be regulated as any diabetic patient without ketosis.

As to the differential diagnosis of acute surgical conditions of the abdomen and ketosis, when a patient is admitted presenting the syndrome which I have outlined and we do not know the diagnosis exactly, my policy has been to postpone the operation if possible until the patient is ketone free. If he is ketone free and the abdominal symptoms persist, then I think he is entitled to an exploratory operation. There is one other test which I have found useful; namely, study of the leukocytes, not their number but rather the characteristic toxic granulation. I recall two instances of diabetic ketosis simulating surgical abdominal involvement without elevation of temperature or pulse rate, and with only 8,000 leukocytes in the peripheral circulation. The abdomen was tender with some rebound tenderness, and many granules were seen in the leukocytes. The acetonuria disappeared after insulin therapy, and as the patient appeared to improve surgical intervention was postponed. After two days of relative quiescence the temperature suddenly rose and an exploration revealed a gangrenous appendix. The other patient showed the classic picture of diabetic ketosis with dominant abdominal symptoms. The leukocyte count was not high, but toxic granules were present. In this case we did not wait too long. Insulin and an infusion were given and an acutely involved appendix was then removed at operation. The patient in whom ketosis is present without abdominal complications may show an even more marked leukocytosis, with a count up to 50,000 and more but, the absence of toxic granulation is conspicuous. I do not wish to convey the thought that the presence or absence of cells containing toxic granules is an infallible guide. It must be evaluated in relation to the other clinical and laboratory data.

HYPOGLYCEMIA

The other diabetic emergency is hypoglycemia. The syndrome which is caused by hypoglycemia is not the same with regular insulin as with protamine zinc insulin. The differentiation is very important. With regular insulin the patient has ample warning. He becomes nervous and apprehensive, begins to sweat, has headache, his memory becomes foggy, there are visual disturbances, and he realizes that something is wrong. Orange juice will correct the difficulty immediately. With protamine zinc insulin the onset of these symptoms is rather insidious. The only trouble may be headache; it may continue for six, eight or ten hours, and then the patient may go precipitously into hypoglycemic coma from which he cannot be aroused. We therefore tell patients who are receiving protamine zinc insulin "If and when you experience any unusual symptoms, no matter what they are, please take some orange juice at once and follow that up with milk and crackers." The reasons for that are probably obvious to all of you. The orange juice will counteract the existing hypoglycemia, while the milk and crackers, a cereal or bread will continue to supply carbohydrate to combat the prolonged action of the protamine zinc insulin.

The preparation of the surgical patient is a problem that all of you will encounter, and it is not difficult. With the emergency surgical condition such as acute appendicitis in diabetes, the patient is taken to the operating room. There he is given an intravenous clysis of 5 per cent dextrose in 1,000 cc. of saline solution, together with 25 units of insulin hypodermically. When he is returned from the operating room, the procedure is repeated. That will insure a flow of urine, which is frequently examined. The dose of insulin which is then given is determined by the rule I have already stated: 25 units if the reaction is yellow, 15 units if it is green, and only orange juice if the patient can take fluids by mouth and the reaction is blue. Continue with that until the patient is able to eat. Then give a simple diet and regulate it in the customary manner.

With the surgical condition in diabetes which is not an emergency, the procedure is slightly different. We all know that patients in the operating room lose a good deal of fluid, and I prefer to hydrate them for a longer period before operation. With those patients we advise the ingestion of table salt in a dose of 1 Gm. (two half gram tablets) every hour with a glass of water, for about ten or twelve hours before operation.

To recapitulate briefly: The most serious emergencies of the diabetic are (1) ketosis and (2) hypoglycemia. The treatment of ketosis is based on two definite scientific principles, the replacement of fluid and salts and the use of insulin. The treatment of hypoglycemia is based on a sound scientific principle as well, the administration of sugar. For the rapidly acting insulin sugar may be given in the form of orange juice and for the slowly acting protamine zinc insulin milk and crackers or some form of carbohydrate that is slowly absorbed so that it can neutralize the prolonged effect of the insulin.

There appears to be more to the mechanism and the treatment of diabetic coma than has been indicated in this discussion. There are factors about which a good deal still needs to be learned. We should not gain the impression that by the treatment outlined we are able to save all patients with diabetic coma. Under the most favorable conditions and the best treatment known, many of the patients still die, for reasons which in the present state of our knowledge remain unknown. This appears to be the general experience.

DISCUSSION OF QUESTIONS

DR. DU BOIS: Do you have much difficulty in getting a patient to take tablets containing salt (sodium chloride)?

DR. TOLSTOI: No.

DR. DU BOIS: How do you give them?

DR. TOLSTOI: Just let the patient swallow the tablet. If he cannot swallow the tablet, crush it and follow it with a drink of water.

DR. HARRY GOLD: One might give about one-sixth teasponful of ordinary table salt, could one not?

DR. TOLSTOI: Yes. We prefer the tablet form. It is convenient. However, salt in any form will do.

DR. MCKEEN CATTELL: Your procedure is based entirely on the matter of replacing salt and fluid which is below normal?

DR. TOLSTOI: That is right. The diabetic patient in coma does not retain dextrose solutions alone for any length of time. The fluid is rapidly lost. The addition of salt helps to fix the fluid in the body. I am sure that some of the hospital staff will recall the patients who have come into the house as little shriveled up individuals and by the next day they seem like balloons, with big puffy cheeks and eyes that seem small, from edema resulting from the salt water treatment. Of course, as soon as the salt is discontinued the water flows off and the patient seems more normal.

DR. SAMUEL B. BARKER: Don't you think that the salt may have some effect in replacing the deficient base and in the differential excretion of chloride perhaps as ammonia chloride? That, of course, would not be a rapid process. Undoubtedly the main thing would be the salt itself, but don't you think the retention of base from the chloride would be an important effect of salt administration?

DR. TOLSTOI: That is quite true, because in these cases acetone is being produced all the time, and to neutralize that we draw on the body's supply of base. There are other points, too controversial, perhaps, to discuss here, namely the administration of sodium bicarbonate, gastric lavage and lactate-Ringer (Hartmann's) solution. I don't recommend them nor do I object to their use.

DR. DU BOIS: Of course, the question as to whether or not sodium bicarbonate should be used is at least thirty years old. The point about keeping the diabetic patient wet is also fairly old. I remember that at least twenty-five years ago Theodore Janeway used to insist on that: the wet diabetic patient did not go into coma.

Dr. Barker, will you continue the discussion of diabetic acidosis?

DR. BARKER: The term "acidosis" is rather unfortunate. It was introduced by Naunyn, who intended it to designate the production in diabetes of beta hydroxybutyric and acetoacetic acids, a situation which is now rather well covered by "ketosis." Acidosis has come to have such broad implications that it is often used to include practically all aspects of the condition resulting from the production of these two acids. The word itself is an exaggeration: the blood is seldom actually acid, in the sense that its p_H falls below 7.0, and often considerable amounts of ketone bodies are found in the blood without any deviation from the normal range of 7.3 to 7.5. Probably the best definition of the present day use of the term is that suggested by Van Slyke and Cullen: a lowered alkali reserve resulting from acid production. In the case of diabetes, acid production would be the production of beta hydroxybutyric and acetoacetic acids.

At the start of this short discussion on diabetic acidosis I should remind you that the fundamental cause of the extensive acid-base disturbances found in diabetes is the deficient carbohydrate oxidation. This leads to a deranged fat metabolism, with large amounts of the ketone bodies being produced from the incomplete oxidation of fatty acids. These are neutralized by means of base taken from $BHCO_3$, the carbon dioxide freed being eliminated by the lungs. The kidneys assist in the attempted regulation of normal equilibrium by excreting the acids partly in the form of free acid and partly in the form of ammonium salts. The kidney is able to form ammonia in order to conserve fixed base (that is, sodium). At this stage no change has yet been produced which is not rather easily reversible by remedying the primary cause, namely the poor oxidation of carbohydrate. The proper procedure is, of course, the administration of carbohydrate and insulin. This will stop the acid production and assist in the oxidation of any accumulated ketone bodies. The base combined with these acids is thereupon released and

serves to return the carbon dioxide combining power of the blood to normal.

However, if the diabetic condition is allowed to continue unabated, the organic acid load increases and the alkali reserve of the blood is still further reduced. Ammonia production by the kidneys is unable to keep up with acid excretion, and the use of fixed base is resorted to. This still further reduces the ability of the blood to carry carbon dioxide and at the same time lowers the total salt concentration. This hypotonicity is at once remedied by the excretion of water until the proper salt concentration is reached. This results in a temporary isotonicity but also produces a lowered total content of electrolyte and a lowered blood volume.

As the condition progresses still further, the amount of base available to carry carbon dioxide becomes small and the base from chloride seems to be freed to neutralize acid material. Hydrochloric acid often is vomited or may be excreted by the kidneys as ammonium chloride. The depletion of alkali and long continued glycosuria eventually lead to serious dehydration, hyperpyrexia and hyperpnea. In the extreme condition of diabetic coma, desiccation is pronounced, blood volume, alkali reserve and base content are very low, and the blood p_H may be below 7.1.

The changes as sketched here have been related to blood but of course apply to all extracellular body fluids. The cells also are hit by the loss of salt and water, but they are most affected by the self destruction induced by the increased breakdown of body protein. All the changes described are gradual; conditions merge into one another with no sharp demarcation. In addition to the tissue changes, there is pronounced dyspnea caused by the need of eliminating large amounts of carbon dioxide aggravated by hyperthermia and sometimes by increased metabolism.

The first line of treatment must still remain the alleviation of the defective carbohydrate oxidation with insulin, coupled with the administration of carbohydrate to replace the lowered body stores. Beyond that, one may look toward restoring the water and the electrolyte balances. The patient is dehydrated but, as Dr. Tolstoi has mentioned, the administration of water alone will not afford any permanent relief. The need for base is acute, but it is undoubtedly best to supply this as sodium chloride rather than as sodium bicarbonate, for two principal reasons: First, there is often a need for chloride as well as for base. If base is needed in larger amounts than chloride, the kidney is quite capable of excreting the excess of chloride as ammonium chloride, and the fixed base is retained. It is furthermore quite possible that the administration of sodium bicarbonate even in extreme diabetic acidosis may overcompensate and cause a dangerous alkalosis, when insulin is also used.

It may be reemphasized that the most logical treatment for the alleviation of diabetic acidosis is the use of insulin plus sugar, combined with salt administration.

STUDENT: I should like to ask Dr. Barker if he considers that the danger of acidosis is due primarily to dehydration.

DR. BARKER: Dehydration certainly is an exceedingly serious aspect of untreated acidosis. The diminished alkali reserve, lowered blood p_H, hyperglycemia and other carbohydrate disabilities, fatty infiltration and degeneration are all important involvements in diabetes and all are precursors of dehydration. But the dehydration and lowered blood volume are undoubtedly the factors which hit the hardest, in the final analysis.

The administration of base was an early treatment, but bicarbonate administration did not help permanently. Magnus Levy's old idea was that one should cause the patient to excrete as much acetone as possible; that it was more important to eliminate it than to keep it. Actually, an excretion of acetone bodies in the urine of a normal persons can be caused by giving a large amount of base.

DR. TOLSTOI: Isn't there a feeling among cardiologists that the reduction of blood volume is detrimental to the heart of the diabetic patient who has lost a lot of fluid and is one of the causes which finally is responsible for death?

DR. EPHRAIM SHORR: With respect to the cardiac accidents, we should remember that the proper function of the heart is dependent on a normal type of metabolism, a situation which does not exist in the absence of insulin. It seems to me that to regard cardiac failures and irregularities that occur as due to just one factor, such as the dehydration, is possibly a little unsafe. In working with hearts of diabetic dogs we have been struck with the rather profound changes which occur in the texture of the muscle. The diabetic heart becomes fragile and shreds easily. There are also some histologic deviations from the normal. Therefore I think more than just one factor is responsible for the failures which occur.

ROLE OF THE PITUITARY

DR. DU BOIS: I will ask Dr. Chambers to tell us something of his work on the role of the pituitary.

DR. WILLIAM H. CHAMBERS: There are several excellent reviews of this subject, by Houssay, in the May 1937 issue of the *American Journal of the Medical Sciences*, also by Long and Britton and by Riddle in the *Cold Spring Harbor Symposia* for the summer of 1937 and a review article by Russell in *Physiological Reviews* for January 1938. These reviews discuss the effects of the different endocrines on diabetes. Many different types of animals, from the toad to the dog, are used and it is difficult to put the data together and form any consistent picture.

The depancreatized dog is in a completely diabetic condition when insulin has been withheld for three or four days, or three or four days after the operation when the animal has been given no food. You are quite familiar with the picture: respiratory quotients of 0.70 to 0.73 in the basal condition and no rise in quotient with the introduction of dextrose. The D:N ratio is 2.8. This condition prevails for about two weeks of fasting, until the animal loses from 45 to 50 per cent of its body weight. At that time the creatine excretion rises very definitely in the depancreatized animal. Sometimes the nitrogen excreting increases. This is associated with a rise in the respiratory quotient to the protein level, indicating that the protein is handled as a normal animal would take care of it.

Barker has studied this condition in our laboratory and found that the rise in the protein metabolism is not an essential part of the picture. At this time the acetone bodies may disappear completely and the D:N ratio may fall to zero, meaning no dextrose excretion at all. When dextrose is given the respiratory quotient shows a rise, indicating that some of the dextrose can be oxidized. Here is a condition where the animal in the absence of insulin can oxidize some sugar.

Now, a similar situation is found, as you know, in the Houssay animal. Houssay in 1929 pointed out that the removal of the pituitary would change the diabetic

picture, lowering the D:N ratio, reducing the ketosis almost to zero and reducing the glycosuria. We studied several animals of this type in the calorimeter with the help of Dr. Chandler and Dr. Sweet and found that the respiratory quotients under basal conditions would range between 0.74 and 0.78. That is, the animals under basal conditions were burning some sugar at all times.

But when we gave them dextrose by mouth the injected sugar apparently was not burned. That is, there was little rise in the respiratory quotient, only five out of fifteen experiments showing any definite increase. About 60 per cent of the sugar was excreted. So we attempted a different type of experiment, one of which may serve as an illustration. The data are from one of nine dogs with which balance studies were made in the following fashion: The animal was given meat twice daily and put in the calorimeter for eight hours during the course of the day. The metabolism when the animal was quiet in the cage at night was probably quite equivalent to that in the calorimeter in the dark during the daytime.

We found that when the animal was on a pure meat diet for five days the D:N ratio was 2.46, that it excreted 40 Gm. of dextrose and the equivalent of 16 Gm. of nitrogen a day and that the respiratory quotient during the day averaged 0.75. This was not changed by the introduction of the meat. On the basis of a respiratory quotient of 0.75, in twenty-four hours the animal would oxidize about 30 Gm. of sugar.

In a subsequent period of three days we added to the meat, given twice daily, 30 Gm. of dextrose and some lard. The animal then excreted about 15 Gm. of the 30 Gm. which was fed over the amount which might be derived from the protein according to the D:N ratio. In other words, the animal was oxidizing 30 Gm. from the protein and 15 more from the extra dextrose, and 15 Gm. was recovered in the urine. The respiratory quotient rose to 0.78. Calculating from the heat production and the respiratory quotient, we find the dextrose oxidized in twenty-four hours to be about 50 Gm.

In a later experiment the animal was given 100 Gm. of dextrose a day for four days and 85 Gm. was excreted; the oxidation remained practically the same and the respiratory quotient about the same.

In other words, these animals lacking a pituitary and a pancreas are able to oxidize a limited amount of dextrose. An increased amount in the diet does not change the amount oxidized, but it is merely excreted.

You recall that Long has removed the adrenals from depancreatized cats and found that the diabetes was ameliorated in much the same way that Houssay showed with the hypophysectomized diabetic dogs. We have studied four adrenalectomized depancreatized dogs. The data from these animals could be put with the data from the Houssay animals and no distinction found. The D:N ratios and the respiratory quotients are about the same. The respiratory quotient shows no particular rise when dextrose is ingested. The removal of the adrenal seems to be quite comparable to the removal of the pituitary as far as carbohydrate oxidation is concerned.

In an article published in 1937, Long reported that adrenal cortex extract given in large amounts to rats which had been partially depancreatized produces a definite glycosuria. In the earlier reports, small amounts of cortical extract showed no influence on carbohydrate metabolism. We are not prepared to say from our data to what extent cortical extract may influence carbohydrate metabolism. In one adrenalectomized depancreatized animal cortical extract was withheld for six days. There was no difference in the carbohydrate metabolism that we could determine.

Another animal was hypophysectomized and studied, and later the adrenals were removed and the same experiments performed. The results were quite comparable.

So the removal of the adrenals after taking out the pituitary apparently does not change the picture further. Long has suggested, I believe, that the pituitary acts through the adrenal cortex. I think that this still remains to be demonstrated.

Now I want to take just a minute to show quantitative relationships in these different animals. The first animal—and these are round figures taken from the experimental data, estimates rather than actual figures—is a normal animal fed with plenty of carbohydrate in the diet. When given 50 Gm. of dextrose, it will absorb about a gram per kilogram hourly in the course of four hours. Of that amount 40 per cent is oxidized and 60 per cent deposited as glycogen. Whenever dextrose is given we find that it is not immediately completely oxidized but is partly deposited as glycogen. The Houssay animal will oxidize about 10 per cent of the dextrose given. According to Houssay's figures about 20 per cent in this four hour period may be deposited as glycogen and the remainder, or about 70 per cent, excreted.

The completely depancreatized animal will oxidize none. Glycogen deposition has been shown to take place in the absence of insulin if the blood sugar is raised to an abnormally high level. But when the dextrose is given by mouth the blood sugar is not high enough to show a definite deposition of the glycogen and 100 per cent of the dextrose can be recovered in the urine.

We see on a quantitative basis that removal of the pituitary, and we might put the adrenal in the same category, does not by any means restore the animal to a normal position, either with respect to oxidation of dextrose or with respect to the deposition of glycogen.

There is one other complicating factor in the relationship of the pituitary and the adrenal. It is apparent from this picture that we did not obtain 100 per cent recovery from the diabetic condition by any means. In two animals we did find practically a complete restoration of ability to oxidize dextrose. One of these was a Houssay animal which showed in the histologic sections a very definite lesion in the region of the hypothalamus but a perfectly normal adrenal cortex so far as we could tell. The other animal was a depancreatized animal which never showed glycosuria. We could find no pancreas at autopsy. The animal burned sugar in normal fashion but the autopsy showed a cyst in the posterior lobe of the pituitary and marked atrophy of the adrenal cortex. So I think that the explanation of the parts played by the pituitary and the adrenal cortex is still decidedly theoretical.

DIABETIC TISSUE

DR. DU BOIS: We have heard about the diabetic patient and the diabetic dog. I wonder if Dr. Shorr will say a little about the diabetic tissue that has been studied.

DR. EPHRAIM SHORR: We have come to regard diabetes as a disturbance of the mechanism by which the various ductless glands regulate sugar metabolism, rather than a defect exclusively associated with an insulin deficiency.

It seems probable that tissues have a fundamental capacity to metabolize a wide variety of foodstuffs, including carbohydrates, which is essentially independent of the secretions of the ductless glands. This is evidenced by the observation that embryonic tissues are capable of sugar oxidation before the ductless glands appear. As organisms became more complex with evolution, the ductless glands developed and assumed control over this function, among others. This loss of independence was one of the penalties the tissues had to pay for their greater complexity and higher organization. It is amazing that, despite the millions of years of such servitude, an organism as well as isolated tissues can still give evidence of this primitive independence and burn sugar without the assistance of insulin.

Some experiments in our laboratory have a bearing on this point. You will recall that Dr. Chambers showed that animals with pancreas and pituitaries removed were capable of oxidizing more carbohydrate than animals with pancreatic diabetes. The improvement was, however, only partial. We studied the respiratory metabolism of tissues isolated from these animals and found that they were capable of an entirely normal sugar metabolism. It is apparent from these experiments in the Houssay animal that there must still exist other factors which inhibit sugar metabolism apart from the pituitary secretions. We then asked ourselves whether the superiority of isolated tissues over the whole animal might not reside in the degradation of these other inhibiting factors with time, when the tissues were removed from the body. This theory was then tested by the study of tissues from diabetic animals in the following manner: They were removed from the animals under sterile conditions. One portion of tissue was studied at once and found, as one might expect, to have no capacity to oxidize sugar. Another portion was incubated for ten hours at body temperature under proper conditions. At the end of ten hours, these tissues were found to have regained the normal capacity to oxidize carbohydrate. This occurred independently of insulin. Our working hypothesis is that during the period of incubation the inhibiting influences, whether pituitary or adrenal in origin, were used up. Now the tissues were free both of the sugar-accelerating hormone (insulin) and the inhibiting hormones and had resumed their innate capacity to oxidize this foodstuff without any hormonal help.

In view of what I have said, you may have been puzzled about the absence of any influence of this conception on the present treatment of diabetes, which you have just heard outlined. What you have heard has been a careful therapeutic regimen based largely on the conception of diabetes in the human being as a disease due to deficient insulin production. This does, indeed, represent a lag between the results of animal experimentation and their application to human disease. It is warranted, however, for the present, on several counts. The chief reason for this apparent disregard of polyglandular factors in human diabetes is that we know but little about the role of the factors, other than insulin. This difficulty in correlating animal experiments with human disease is also seen in exophthalmic goiter, in which, despite our considerable knowledge of the presence of thyrotropic pituitary factors which produce a comparable condition in animals, little or nothing is known of the way in which these pituitary factors act in the production of exophthalmic goiter.

We must also recognize that, while human disease is in many instances comparable to that produced in animals, there is a tendency for conditions in the human body to become more stable after an initial disturbance than in animals, where it is possible to influence the ductless glands in a much more profound manner. This stabilization of the human organism can also be seen in disturbances of sex physiology, in whose treatment various hormonal principles, particularly those of pituitary origin, have been much less successful than in animals.

Finally, there is some suggestion from the work of Young as to the way in which these two points of view, the polyglandular disorder as against the relatively stable metabolic disturbance dominated by one secretion, can be reconciled. Young has been able, by injection of pancreatic extracts into animals, to produce degenerative changes in the pancreas which are followed by diabetes. This diabetes differs in no way from the diabetes produced in animals by complete removal of the pancreas and is, once degeneration is extreme, a relatively stable condition. This state produced by pancreatic extracts might be the prototype of human diabetes.

The newer conception of diabetes, however, is so recent and so inadequately explored in the human being up to the present that we should not be discouraged about the fact that it is not reflected in our standard treatment of the disease. A few years may well bring about an entirely new picture as a result of insight gained into the possible mechanisms underlying this disease.

NATURE OF INSULIN

DR. DU BOIS: I would appreciate it if Dr. du Vigneaud would make a few comments on the present stage of development of the chemistry of insulin.

DR. VINCENT DU VIGNEAUD: Insulin is a protein. The molecule is made up of amino acids, and of such a number of amino acids that immediately the possibility of synthesis is out of the question at present. When you hear individuals talking about synthetic insulin you can rest assured that they have no concept of the subject, because that is out of the question at the present stage of development. Probably no subject in the field of biochemistry is at present being attacked more diligently than the chemistry of the proteins. It is particularly interesting to note that various laboratories of classic physical chemistry which just a few years ago would not think of working on a biologic substance are working on proteins from a physicochemical standpoint. This is indeed a significant development. Anything done on the chemistry of proteins will in turn throw light on the chemistry of insulin. Also anything done on the chemistry of insulin in turn has its significance to the chemistry of proteins.

The fact that insulin is a large protein molecule with molecular weight of about 35,000 leaves the hope of oral administration at the present time somewhat discouraging. It is true that insulin is destroyed by certain proteolytic enzymes, but that is not such a formidable barrier as the size of the molecule because there are various ways to get around the enzyme destruction. The real problem is the fact that the molecule is so large that it is difficult for appreciable amounts to pass through the membrane of the intestine. One approach is to attempt to dissociate this large molecule into smaller units and still retain activity.

An interesting chemical development has been the recognition by many that zinc must be present in order to obtain a form of crystalline insulin. The crystalline insulin is a zinc complex of this protein. Much work

has been done to find out whether other metals will serve. Of all the other metals that have been tried, cadmium, cobalt and nickel are the only ones that enable the insulin to be crystallized. The crystallization of insulin is now so successful that it is being done commercially and a solution of crystalline insulin is on the market. The relationship of these metals to the insulin and the nature of the linkage are attracting the attention of our group and many others.

Much work is still going forward on the composition of insulin. The entire insulin molecule is still not completely accounted for. Considerable work is also going forward on various physicochemical properties of this interesting protein.

STUDENT: Why is zinc used rather than any of the other metals you mentioned?

DR. DU VIGNEAUD: The fact that zinc was the first metal to be encountered in the work is perhaps one of the reasons. Furthermore, the pancreas contains a considerable amount of zinc and this likewise might have influenced the choice of zinc. The crystals we have so far made with cobalt are tinged a light pink and the nickel crystals have had a green tinge. The fact that the zinc crystals are colorless and the fact that zinc occurs in the pancreas are perhaps the main factors in favor of the choice of zinc.

DR. CATTELL: Is it known how the zinc acts to change the character of the molecule in relation to the matter of absorption?

DR. DU VIGNEAUD: Insulin free of zinc is physiologically active. If you assay one against the other carefully you do not find much difference in spite of the claims to the contrary. However, there is a real difference between protamine insulin and insulin. It is suspected that zinc aids in the combination of protamine and insulin. If there is any difference between zinc insulin and zinc free insulin, which as I say is questionable, I think it would rest on the possibility that zinc insulin has more of a chance of attaching itself to certain proteins at the site of injection and delaying absorption a little bit.

SUMMARY

DR. DU BOIS: Dr. Gold, will you close the conference with a brief summary of the ground covered?

DR. GOLD: In the conference today we have had an account of some of the fundamental background of diabetes. The concept of the mechanism of this disease has undergone revision. Some of the crucial experiments were related which signify that so-called pancreatic diabetes may really represent an endocrine imbalance in which several endocrine organs are involved, the pancreas, the pituitary and the adrenal. This is in line with the observation to which Dr. Shorr called our attention, that diabetic tissue possesses an innate capacity to oxidize foodstuffs without the intervention of hormones, and that the hormones serve chiefly to regulate this function.

How matters stand now in relation to the chemistry of insulin was considered by Dr. du Vigneaud. Insulin has not been synthesized. It is a protein, and its synthesis awaits further knowledge of the chemistry of proteins. Insulin has a very large molecule, a fact which probably provides a barrier to its absorption from the gastrointestinal tract. There is indication that zinc is essential for the crystallization of insulin. We have been told that enterprise in the field of insulin chemistry is extremely active.

A method for the clinical management of the diabetic patient was outlined in which freedom from symptoms, the maintenance of body weight and the absence of acetone in the urine are regarded as the significant indexes of satisfactory control of the diabetic. Little attention is paid to the level of the blood sugar or the amount of sugar excreted in the urine. These patients are treated with a single daily dose of protamine zinc insulin sufficient to enable them to metabolize enough carbohydrate for their needs.

The treatment of the two important diabetic emergencies and their physiologic mechanisms were discussed, namely, coma due to ketosis and insulin shock. The conspicuous symptoms of ketosis were considered: the parched tongue and the dry and flushed skin, headaches, pain in the calves of the legs, and abdominal symptoms suggesting surgical abdomen. Emphasis was placed on the necessity for large quantities of fluid, salt and insulin in controlling diabetic ketosis. The symptoms of overdosage in the case of protamine zinc insulin are somewhat different from those in the case of the regular insulin, and more protracted treatment is necessary in the case of the former to insure against recurrence of the symptoms of shock because of the longer duration of action of the protamine zinc insulin.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

ANTIPNEUMOCOCCIC SERUMS

(See General Article, N. N. R., 1940, p. 429)

Antipneumococcic serum obtained from rabbits has been shown to possess less of certain disadvantages accompanying the use of serum obtained from horses. Rabbit serum furnishes antibodies of smaller molecular size, which are therefore expected to penetrate infected tissues more readily. A method has been devised to minimize reactions, an attribute of nearly all natural (raw) rabbit serum. Chills are reportedly somewhat more common with unconcentrated than with concentrated rabbit serum, but these have been modified by the oral administration of acetylsalicylic acid (0.9 Gm.) immediately before the serum is given. As with horse serum, all preliminary sensitivity tests for susceptibility to rabbit protein should be performed. The Council has recognized as acceptable only those antipneumococcic types of rabbit serum for which horse serum has been accepted for N. N. R. (I, II, IV, V, VII, VIII). With the exception of type IV, only these types of horse and rabbit serum are included in the U. S. Pharmacopeia. "The outside label must bear the name Antipneumococcic Serum *and the specific type of pneumococcus represented, the genus of animal employed, when other than the genus Equus,* the manufacturer's lot number of the serum, the name, address and license number of the manufacturer, and a statement of the date beyond which the Serum may not be expected to retain the potency prescribed by the governmental authority." *U. S. P.*

ANTIPNEUMOCOCCIC SERUM, TYPE I (FROM RABBITS).—"Obtained from the blood of an animal . . . of the genus Lepus, which has been immunized with cultures of a pneumococcus (Diplococcus pneumoniae) of one of the varieties known as type I . . ." *U. S. P.*

For standards see the U. S. Pharmacopeia XI, 1939, Second Supplement, under Serum Antipneumococcicum.

Dosage.—"Average Dose-Therapeutic, by parenteral injection, from 20,000 to 100,000 units." *U. S. P.*

Initial and subsequent dosage should be administered by such route, in such amount and at such intervals as indicated by the age and condition of the patient, according to the judgment of the physician. With a large initial dose, fewer units may be curative. The Francis cutaneous test (injection of specific pneu-

mococcic capsular polysaccharide) may be used in conjunction with clinical observations to determine adequacy of dosage.

The Gilliland Laboratories, Inc., Marietta, Pa.

Antipneumococcic Rabbit Serum, Therapeutic, Type I.—Prepared by immunizing rabbits with intravenous injections of virulent cultures of type I pneumococcus. Cultural virulence is maintained by frequent passage through mice. When trial bleeding shows the serum to have reached a sufficient degree of potency, the rabbits are bled aseptically and the serum is collected, refined and concentrated by a method perfected in the firm's laboratories. After concentration the usual sterility and safety tests are carried out in accordance with the requirements of the National Institute of Health. The potency of the product is expressed in terms of the unit as described by Felton (*J. Infect. Dis.* **37:** 199 [Sept.], 309 [Oct.] 1925; *J. A. M. A.* **94:** 1893 [June 14] 1930), the unit being one-three hundredth cc. of the control serum distributed by the National Institute of Health. The serum is marketed in ampule packages, each containing 20,000 units or 50,000 units of type I pneumococcus antibody.

E. R. Squibb & Sons, New York.

Antipneumococcic Rabbit Serum, Type I, Concentrated.—Prepared from the blood of rabbits which have been immunized by repeated injections of type I pneumococci, according to the procedure suggested by Horsfall, Goodner, MacLeod and Harris (*J. A. M. A.* **108:** 1483 [May 1] 1937). After four to six weeks of immunization, the rabbits are bled from the heart, the fluid portion of the blood is separated from the corpuscles, and the antibody in the fluid is refined and concentrated by salting out with ammonium sulfate, the globulin fraction being retained. The final product contains merthiolate 1 in 10,000 and 0.2 per cent of phenol. The resulting solution is then tested in comparison with the standard antipneumococcic serum distributed by the National Institute of Health to determine the number of units of type I specific serum per cubic centimeter. It is then filtered through a Berkefeld filter and again tested for potency. After the results of the assay are known, it is filled under aseptic precautions into sterile vials, each containing at least 50,000 units. Marketed in packages of one vial containing 20,000 units and one vial containing 5 cc. of the same serum diluted (1:100) for the sensitivity test.

ANTIPNEUMOCOCCIC SERUM, TYPE II (FROM RABBITS).—"Obtained from the blood of an animal . . . of the genus Lepus, which has been immunized with cultures of a pneumococcus (Diplococcus pneumoniae) of one of the varieties known as . . . type II . . ." *U. S. P.*

For standards see the U. S. Pharmacopeia XI, 1939, Second Supplement, under Serum Antipneumococcicum.

Dosage.—"Average Dose-Therapeutic, by parenteral injection, from 20,000 to 100,000 units." *U. S. P.*

Initial and subsequent dosage should be administered by such route, in such amount and at such intervals as indicated by the condition of the patient, according to the judgment of the physician. With a large initial dose, fewer units may be curative. The Francis cutaneous test (injection of specific pneumococcic capsular polysaccharide) may be used in conjunction with clinical observations to determine adequacy of dosage.

The Gilliland Laboratories, Inc., Marietta, Pa.

Antipneumococcic Rabbit Serum, Therapeutic, Type II.—Prepared by immunizing rabbits with intravenous injections of virulent cultures of type II pneumococcus. Cultural virulence is maintained by frequent passage through mice. When trial bleeding shows the serum to have reached a sufficient degree of potency, the rabbits are bled aseptically and the serum is collected, refined, and concentrated by a method perfected in the firm's laboratories. After concentration the usual sterility and safety tests are carried out in accordance with the requirements of the National Institute of Health. The potency of the product is expressed in terms of the unit as described by Felton (*J. Infect. Dis.* **37:** 199 [Sept.], 309 [Oct.] 1925; *J. A. M. A.* **94:** 1893 [June 14] 1930), the unit being one-one hundred and fiftieth cc. of the control serum distributed by the National Institute of Health. The serum is marketed in ampule packages, each containing 20,000 units or 50,000 units of type II pneumococcus antibody.

ANTIPNEUMOCOCCIC SERUM, TYPE V (FROM RABBITS).—"Obtained from the blood of an animal . . . of the genus Lepus, which has been immunized with cultures of a pneumococcus (Diplococcus pneumoniae) of one of the varieties known as . . . type V. . . ." *U. S. P.*

For standards see the U. S. Pharmacopeia XI, 1939, Second Supplement, under Serum Antipneumococcicum.

Dosage.—"Average Dose-Therapeutic, by parenteral injection, from 20,000 to 100,000 units." *U. S. P.*

Initial and subsequent dosage should be administered by such route, in such amount and at such intervals as indicated by the condition of the patient, according to the judgment of the physician. With a large initial dose, fewer units may be curative. The Francis cutaneous test (injection of specific pneumococcic capsular polysaccharide) may be used in conjunction with clinical observations to determine adequacy of dosage.

The Gilliland Laboratories, Inc., Marietta, Pa.

Antipneumococcic Rabbit Serum, Therapeutic, Type V.—Prepared by immunizing rabbits with intravenous injections of virulent cultures of type V pneumococcus. Cultural virulence is maintained by frequent passage through mice. When trial bleeding shows the serum to have reached a sufficient degee of potency, the rabbits are bled aseptically and the serum is collected, refined and concentrated by a method perfected in the firm's laboratories. After concentration the usual sterility and safety tests are carried out in accordance with the requirements of the National Institute of Health. The potency of the product is expressed in terms of the unit, based on satisfactory protection tests in mice. The unit is one-five hundredth cc. of the control serum distributed by the National Institute of Health, for type V pneumococcus antibody. The serum is marketed in ampule packages, each containing 20,000 units or 50,000 units of type V pneumococcus antibody.

ANTIPNEUMOCOCCIC SERUM, TYPE VII (FROM RABBITS).—"Obtained from the blood of an animal . . . of the genus Lepus, which has been immunized with cultures of a pneumococcus (Diplococcus pneumoniae) of one of the varieties known as . . . type VII. . . ." *U. S. P.*

For standards see the U. S. Pharmacopeia XI, 1939, Second Supplement, under Serum Antipneumococcicum.

Dosage.—"Average Dose-Therapeutic, by parenteral injection, from 20,000 to 100,000 units." *U. S. P.*

Initial and subsequent dosage should be administered by such route, in such amount and at such intervals as indicated by the condition of the patient, according to the judgment of the physician. With a large initial dose, fewer units may be curative. The Francis cutaneous test (injection of specific pneumococcic capsular polysaccharide) may be used in conjunction with clinical observations to determine adequacy of dosage.

The Gilliland Laboratories, Inc., Marietta, Pa.

Antipneumococcic Rabbit Serum, Therapeutic, Type VII.—Prepared by immunizing rabbits with intravenous injections of virulent cultures of type VII pneumococcus. Cultural virulence is maintained by frequent passage through mice. When trial bleeding shows the serum to have reached a sufficient degree of potency, the rabbits are bled aseptically and the serum is collected, refined and concentrated by a method perfected in the firm's laboratories. After concentration the usual sterility and safety tests are carried out in accordance with the requirements of the National Institute of Health. The potency of the product is expressed in terms of the unit, based on satisfactory protection tests in mice. The unit is one-nine hundredth cc. of the control serum distributed by the National Institute of Health, for type VII pneumococcus antibody. The serum is marketed in ampule packages, each containing 20,000 units or 50,000 units of type VII pneumococcus antibody.

ANTIPNEUMOCOCCIC SERUM, TYPE VIII (FROM RABBITS).—"Obtained from the blood of an animal . . . of the genus Lepus, which has been immunized with cultures of a pneumococcus (Diplococcus pneumoniae) of one of the varieties known as . . . type VIII." *U. S. P.*

For standards see the U. S. Pharmacopeia XI, 1939, Second Supplement, under Serum Antipneumococcicum.

Dosage.—"Average Dose-Therapeutic, by parenteral injection, from 20,000 to 100,000 units." *U. S. P.*

Initial and subsequent dosage should be administered by such route, in such amount and at such intervals as indicated by the condition of the patient, according to the judgment of the physician. With a large initial dose, fewer units may be curative. The Francis cutaneous test (injection of specific pneumococcic capsular polysaccharide) may be used in conjunction with clinical observations to determine adequacy of dosage.

The Gilliland Laboratories, Inc., Marietta, Pa.

Antipneumococcic Rabbit Serum, Therapeutic, Type VIII.—Prepared by immunizing rabbits with intravenous injections of virulent cultures of type VIII pneumococcus. Cultural virulence is maintained by frequent passage through mice. When trial bleeding shows the serum to have reached a sufficient degree of potency, the rabbits are bled aseptically and the serum is collected, refined and concentrated by a method perfected in the firm's laboratories. After concentration the usual sterility and safety tests are carried out in accordance with the requirements of the National Institute of Health. The potency of the product is expressed in terms of the unit, based on satisfactory protection tests in mice. The unit is one-two hundred and fiftieth cc. of the control serum distributed by the National Institute of Health, for type VIII pneumococcus antibody. The serum is marketed in ampule packages, each containing 20,000 units or 50,000 units of type VIII pneumococcus antibody.

POLLEN EXTRACTS-CUTTER (See New and Nonofficial Remedies, 1940, p. 43).

The following additional forms of Pollen Extracts-Cutter have been accepted:

Acacia; Alder; Alfalfa; Alkali Rye Grass; Almond; Annual Blue Grass; Aspen; Barley; Bent Grass; Birch; Bract Scale; Brome Grass; Broncho Grass; Canada Blue Grass; Chapparal Broom; Cheat Grass; Chrysanthemum; Clover; Coreopsis; Cosmos; Cultivated Rye; Curly Dock; Dahlia; Dandelion; Date; Deodar Cedar; Elm; English Walnut; Eucalyptus; False Coastal Ragweed; Field Oats; Field Wheat; Goldenrod; Greasewood; Hops; Incense Cedar; Koehler's Grass; Locust; Mesquite; Mexican Tea; Monterey Cypress; Mountain Sagebrush; Mustard; Pasture Sagebrush; Pecan; Perennial Rye Grass; Pickleweed; Poverty Weed; Prairie Sagebrush; Privet; Quack Grass; Rabbit Brush; Rose; Salt Grass; Shasta Daisy; Sheep Sorrel; Slender Wheat; Southern Ragweed; Spearscale; Spiny Amaranth; Squirrel Tail; Sugar Beet; Sunflower; Sweet Vernal; Sycamore; Tall Oat Grass; White Valley Oak; Willow; Yellow Pine.

SILVER PICRATE-WYETH'S (See New and Nonofficial Remedies, 1940, p. 486).

The following dosage forms have been accepted:

Soluble Trituration Silver Picrate 20% with Boric Acid 80%: A soluble mixture of silver picrate-N. N. R. (20 per cent) and boric acid (80 per cent).

Silver Picrate Jelly, 0.5 Per Cent: A water miscible jelly containing silver picrate-N. N. R., 0.5 per cent in tragacanth jelly, 1.5 per cent.

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SATURDAY, AUGUST 10, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.

2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.

3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.

4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.

5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.

6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.

7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.

8. Expansion of public health and medical services consistent with the American system of democracy.

ELECTRICAL CONVULSION TREATMENT OF MENTAL DISORDERS

Since the convulsive treatment of schizophrenia was introduced by Meduna in 1934, many excellent results have been reported in the treatment of various psychoses with this technic. Moreover, the insulin-induced hypoglycemic shock described by Sakel has also had wide application. Now comes another variant of convulsive irritative therapy in the form of an electrically induced epileptic fit. In 1937 an Italian physician, Cerletti,[1] reported to the Psychologic Congress at Milan that an electric current passed through the head of a dog produced a typical epileptic fit. His collaborator, Bini, asserted that the brain of a dog had tolerated, without any apparent damage, a current of 3,000 milliamperes. The animal died when the duration of the passage of the current was prolonged to sixty or ninety seconds. Bini believes that the duration of the passage of the current is more important from the point of view of any damage done to the tissue of the brain than the tension of the current. However, many physicians and physiologists who have had experience with such technics consider the assertion unbelievable and feel that under any circumstances the passing of electric current through the brain is a most hazardous procedure.

After much work on the technical details of their method, Cerletti and Bini[1] applied the method to patients with schizophrenia. They report that the electrically induced shock was characterized by an immediate and absolute loss of consciousness, which was followed in from two to four seconds by a convulsive fit. The patients are said to have slept longer than after metrazol shock and to have been of good spirits on awakening. The authors also report that the patients had no recollection of their experience and that the state of excitation frequently observed with metrazol therapy was absent. In some instances the shocks were repeated after several minutes. In a later report Fleming[2] describes the apparatus used and the technic of induction shock. The chief advantage claimed for electrical shock over metrazol shock is the instantaneous loss of consciousness and an absence of such surgical complications as dislocations, which occur with metrazol therapy. Some investigators,[3] however, fail to see much difference in the incidence of complications with the two methods, and Bingel and Meggendorfer[4] particularly report dislocations of the jaw and the shoulder joint and fracture of the humerus and the scapula. Various investigations both in this country and abroad indicate that at least 1,000 persons have already been subjected to this technic.

In the meantime the possibility of serious danger associated with such a technic should not be overlooked. The passing of electric current through the body is always a matter for careful consideration. If the heart is included within the field, low tension currents are dangerous. True, if a current is passed from one to the other side of the head the percentage of current passing through the heart is much less than if the current is passing from arm to leg. In many studies which have been made on the effect of electric current on the brain it has been shown that, when the source of the current is a spark coil at 140 cycles per second with a peak voltage at the break of 220 volts and a resistance of the animal body of 1,640 ohms, a duration varying from three to fifty seconds may result in capillary hemorrhages, ganglion cell changes of swelling and

1. Cerletti, U., and Bini, L.: Boll. Acad. med. rom. **64**: 36, 1938.

2. Fleming, G. W.; Golla, F. L., and Walter, W. G.: Electric-Convulsion Therapy of Schizophrenia, Lancet **2**: 1353 (Dec. 30) 1939.

3. Sogliani, Giorgio: Eine neue Methode der Krampftherapie: die Elektroshocktherapie, Deutsche Ztschr. f. Nervenh. **149**: 159 (Nos. 3 and 4) 1939. Braunmuhl, A.: Der Elektrokrampf in der Psychiatrie, München. med. Wchnschr. **87**: 511 (May 10) 1940. Bingel and Meggendorfer.[4]

4. Bingel, A., and Meggendorfer, F.: Ueber die ersten deutschen Versuche einer Elektrokrampfbehandlung der Geisteskrankheiten, Psichiat.-neurol. Wchnschr. **42**: 41 (Feb.) 1940.

shrinkage satellitosis, gliosis and demyelinization. Morphologic changes in the brain may of course occur with both insulin and metrazol shock therapy. Sufficient data are apparently not yet available to determine whether irreversible changes are produced in patients after several shocks.

It should be obvious from what has been said that electrical shock to the human body may produce fundamental changes in the tissues which are sufficient to threaten life itself. Certainly before extensive clinical application is made of the passage of electric current through the brain, careful histopathologic studies of the brain under varying conditions should be attempted. Finally, the Council on Physical Therapy may well give careful study to the various devices employed in this technic with a view to checking the adequacy of safeguards over the current and voltage and technic of application involved in this procedure.

SICKNESS ABSENTEEISM IN INDUSTRY

The fundamental objective of industrial hygiene is to reduce loss of time, absenteeism and short work spans in industry. In a recent report before the Air Hygiene Foundation, Lanza and Vane [1] called attention to the importance medically and economically of industrial absenteeism in this country. Employers have on the whole been indifferent about lost time from sickness or injury not associated with work as a cause, since disability of this type is not compensable under the law and the costs are difficult to assay. However, evidence from a variety of sources indicates that losses in wages and through disruptions in production schedules must be estimated in billions of dollars each year. Records of sickness benefit associations provide the best available statistical information on lost time in industry. Even these records are frequently of limited value either as an index of incidence or for purposes of comparison. Bookkeeping methods in different industries and occasionally in different units of the same industry are based on totally different conceptions of recording absences. Furthermore, disabilities lasting less than one week are seldom reported since they are not eligible for benefits. Other variables involve sex, age, income and home surroundings of workers, all of which may have greater importance in the production of disability than the nature of the work.

The most reliable available data indicate that the average worker in the United States loses something over nine days annually to disabling sickness. As a rule there will be more sickness among women employees than among men both as to frequency and as to duration and more among married than among single women. Of this total about one day of absence is caused by industrial accidents and occupational diseases. The remainder of the lost time is due to diseases and complaints not directly associated with work as a cause and which make up the bulk of general practice everywhere. These proportions appear to be roughly correct whether the absences are of longer or of shorter duration. True, many of the short term absences are chargeable to personal reasons rather than to sickness. Lanza and Vane support the observation that sickness-prone individuals exist. Although they constitute a small percentage of total employees, they account for an inordinately large number of lost days from illness. So far it has not been possible to associate sick proneness and accident proneness, although it is suggested that some correlation may exist. Rigid standards of preemployment physical examination are not the solution, since even in such physically picked groups as the military services noticeable degrees of absenteeism are encountered.

Lanza concludes that industrial sick absenteeism can be reduced by intelligent coordination of effort between employer, worker and the medical profession. Much reliance must be placed on the private physician, since so many of the causes of lost time fall directly in the province of private practice. Plans are now being formulated designed to provide means for the uniform reporting and recording of all absences in industry no matter what the cause or the duration. Progress in reducing sick absenteeism will take a large step forward as these procedures are generally adopted. The medical profession can make a considerable contribution to knowledge of disease frequency and severity both in industry and in the general population by cooperating in these developments.

1. Sick Absenteeism in Industry, Bull. 4, Medical Series, Air Hygiene Foundation, Inc., Pittsburgh.

Current Comment

BIRTHDAY VOLUME FOR FRANK HOWARD LAHEY

The many friends, both lay and medical, of Frank Howard Lahey have just published a birthday volume [1] in his honor. It is dedicated with the following statement:

> All men desire to be immortal but few fulfil that desire in life. Yet fame gives immortality; and to have attained immortality in sixty short years is an enviable achievement.
>
> We of the medical profession, partakers of that fame which you have gained for us no less than for yourself, offer to you this birthday volume, in which you will find yourself reflected more often than we intend to confess. You have honored medicine, and medicine delights to honor you. This is our birthday gift to you, our friend, adviser, and inspiration.
>
> Yet we alone could not have made this offering. You have been a friend to many. It is fitting, therefore, that some of those to whom you have been physician, healer, and friend, should have made possible the publication of this volume. With it, they also offer homage to one of whom it may be said:
>
> I am a man who has many friends . . .
> And many friends have me.

The book contains principally scientific discussions dealing with surgery. There is, however, one exceptional essay on group medicine and the Lahey Clinic

1. Frank Howard Lahey Birthday Volume. Springfield, Ill., Charles C. Thomas, 1940.

which points out that there is no standardized form of group practice, that private groups are as diversified as hospitals, medical schools or universities, and that the Lahey group is one which has become particularly distinguished for its contribution to medical education and medical investigation. The volume is in its appearance and in its contents distinctive among publications of this type. It honors a physician whom all of us have just honored by his election to the Presidency of the American Medical Association.

COMMITTEE ON HEALTH RESORTS GATHERS INFORMATION

Pursuant to the action of the House of Delegates, the Board of Trustees of the American Medical Association appointed a committee of five to be known as the American Medical Association Committee on American Health Resorts.[1] The purpose of this committee is to collect and compile information on so-called health resorts, which are defined by the committee as follows:

> An institution or region which gives major attention to the use of the special climatic and other natural therapeutic resources, including mineral waters, peloids (moor baths), etc., with which it is endowed by reason of its location. While the use of the natural resources is the prime object or purpose of the institution, other remedies may be applied as an adjunct.

The information collected by a questionnaire devised by the committee, and now in the mail,will be assembled temporarily in the committee's office in the Bureau of Health Education. A list of institutions to receive questionnaires has been compiled from records available in the headquarters office of the Association and from other sources. Such a list is not complete. The committee therefore desires to request that physicians, and the superintendents of institutions of the type described in the definition, communicate the names of such institutions to the Committee on American Health Resorts, American Medical Association, 535 North Dearborn Street, Chicago. Questionnaires will be mailed on receipt of names of institutions. The primary purpose of the committee at present is to assemble information on all institutions of the nature described.

YOUTH LOOKS AT CANCER

The Westchester Cancer Committee, Bronxville, N. Y., has prepared a book[1] designed to inform boys and girls of high school age about cancer. The little book, attractively printed and illustrated, can be read easily in thirty minutes and it provides in brief, condensed form all the essential information about cancer. The Westchester Cancer Committee believes that the high school student "faces the problem without fear and consequently, if informed at this most receptive time of his life, will handle with intelligence a cancer problem coming into his later life. He will also take home correct information to parents, many of whom are unable to read English." This attack on the cancer problem is in line with the feeling of many persons experienced in health education who believe that the so-called adult type of health education, as distinguished from formal instruction in elementary schools, is most effective when concentrated on students of high school age. At this age young minds are fresh and, despite their pose of boredom with education, they are keen to learn what really interests them. Cancer, although curable in its early local stage, continues to increase. The educational movement for the control of cancer is still young as modern public health movements go. It will require at least another decade to make an appreciable impression on the mass of ignorance, prejudice, superstition and fear which surrounds cancer in the public mind.

1. The members of the committee are Dr. Bernard M. Fantus, professor of therapeutics, University of Illinois College of Medicine, Chairman (deceased); Dr. Walter S. McClellan, medical director Research Division, Saratoga Springs Commission, Saratoga Springs, N. Y.; Dr. William P. Holbrook, 4 East Congress Street, Tucson, Ariz.; Dr. Miletus B. Jarman, medical director the Homestead, Hot Springs, Va.; Dr. Euclid M. Smith, Medical Arts Building, Hot Springs National Park, Ark.

1. Youth Looks at Cancer, by the Westchester Cancer Committee, New York: Brookville Press, Inc., Brookville, N. Y., 1940, price 75 cents.

INFANT AND MATERNAL MORTALITY AMONG NEGROES

In each of eight states there are more than 10,000 Negro births annually. As in other aspects of public health, the separation of figures on infant mortality among Negroes from the often considerably different conditions among the white populations of the same areas is of fundamental importance in evaluating actual conditions and needs existing. Tandy,[1] in a recently released statistical study of infant and maternal deaths of Negroes in the United States, points out that more than half (55 per cent) of the Negro births are attended by nonmedical persons—generally untrained or poorly trained midwives. Indeed in seven states, roughly those with the largest Negro populations, midwives attend more than two thirds of the Negro births. Of the 21,000 Negro infants who die each year in the United States, 11,000 die in the first month of life. Natal and prenatal causes are responsible for 41 per cent of the deaths, respiratory diseases for 19 per cent, gastrointestinal conditions for 11 per cent, all other diseases for 13 per cent and unknown and ill defined conditions for 16 per cent. Probably adequate antepartum and postpartum care would materially reduce this infant mortality. This condition is, moreover, paralleled by the maternal mortality rate for Negroes—a rate during the period of 1936 to 1938 of more than double that for white women. This is also susceptible of improvement through better antepartum and intrapartum care. The instruction and supervision of midwives have already begun to show some effect on the trend of infant and maternal mortality among Negroes. The improvement already manifest can doubtless be further extended; the development of consultation services, for example, should be of practical value. This study furnishes a much more satisfactory basis for constructive work in medical care than less critical statistical reports which fail to differentiate between particular groups of the population and their specific health needs.

1. Tandy, Elizabeth C.: The Health Situation of Negro Mothers and Babies in the United States, U. S. Department of Labor, Children's Bureau, Washington, D. C., July 1, 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

COMMITTEE ON MEDICAL PREPAREDNESS

Report of Meeting Held at American Medical Association Headquarters, July 19, 1940

The following were present:

Dr. Irvin Abell, Chairman,
Dr. Charles A. Dukes,
Dr. Roy W. Fouts,
Dr. Stanley H. Osborn,
Dr. John H. O'Shea,
Dr. James E. Paullin,
Dr. Walter G. Phippen,
Dr. Fred W. Rankin,
Dr. Harvey B. Stone,
Dr. Samuel E. Thompson,
Dr. Arthur W. Booth,
Dr. Nathan B. Van Etten,
Dr. Olin West,
Dr. Morris Fishbein

and, by invitation, Dr. Thomas Parran, Surgeon General of the Public Health Service; Colonel Love, United States Army Medical Corps; Colonel Gibson, United States Army Medical Corps; Captain Sutton, United States Navy Medical Corps; Dr. R. G. Leland, Bureau of Medical Economics; Dr. William D. Cutter, Council on Medical Education and Hospitals, and Dr. C. M. Peterson, Council on Industrial Health.

In opening the session Drs. West, Abell and Fishbein discussed the necessity for coordination of various activities such as those of the governmental services, National Research Council, Advisory Committee on National Defense and the American Red Cross in order to avoid a considerable amount of confusion, which is already apparent.

THE QUESTIONNAIRE

Dr. West reported the work of the Committee up to the time of the meeting, including the development of the questionnaire, and reported that 165,000 questionnaires had already been distributed. It is evident that much editing and checking will be required in the handling of the questionnaires. There will also be the necessity for a considerable amount of follow-up in order to secure complete returns.

NEED FOR COORDINATION

Attention was called to the fact that many organizations of physicians had offered their services through the Committee, including the American Heart Association, the National Organization of Women Physicians, the National Medical Association and similar bodies. Apparently some of these associations had been specifically asked by various governmental agencies to undertake certain projects. It was voted that a message be drafted and sent to the Advisory Committee on National Defense and to the President, calling attention to the fact that the Committee on Medical Preparedness meeting with representatives of governmental agencies already finds evidence of duplication of effort and of much confusion and that it is felt that the early appointment of a coordinator for medical and health services is greatly desired in order to speed mobilization of medical resources for any emergency.

Dr. West then reported to the Committee the names of the physicians selected as chairmen for the various states. These were approved as published in THE JOURNAL for August 3.

INFORMATION ON MEDICAL PREPAREDNESS

Plans were developed for extending information developed through the Committee on Medical Preparedness to the medical profession through the use of the editors of the various state journals and the executive secretaries of the various state medical associations. It was pointed out that in several states committees on medical preparedness have already been developed and are functioning. In some states return postal cards have been sent to each member of the state medical association urging immediate return of the questionnaire and asking the member to return the postal card indicating that he has responded.

Other problems discussed at the morning session concerned a request from the British embassy for American physicians who wish to serve in Great Britain, the problems of aviation medicine, the use of refugee physicians and the support of medical education.

VACANCIES IN MILITARY MEDICAL SERVICE

Representatives of the Army and Navy Medical Corps pointed out that there are already vacancies both in the regular corps and in the reserves. The Navy particularly requires younger men in the lower grades in the reserves—especially in the capacity of junior and senior lieutenant.

The problems of industrial medical service were discussed, especially the need for training men for such positions.

An extended discussion was also held on the organization of the reserve corps and on physicians who would be available through membership in these reserve corps. Representatives of the Army, Navy and United States Public Health Service reported the work carried on to the present, involving relationships with other organizations such as the American Psychiatric Association, the American Public Health Association and similar groups.

NEED FOR PHYSICIANS TO CONDUCT EXAMINATIONS

There was indication of the need of physicians in relationship to physical examinations of young men in vocational training, WPA workers and those associated with the National Youth Administration.

TRAINING OF INDUSTRIAL PHYSICIANS

It was proposed that a resolution be developed requesting funds to permit the United States Public Health Service to aid in the training of industrial physicians and to cooperate with various schools of industrial medicine for this purpose.

Also discussed was the question of the use of part-time consultants by various services.

EXEMPTION OF STUDENTS, INTERNS AND RESIDENTS

A resolution was prepared and sent to the Advisory Committee on National Defense and to the President, to Congress and to various governmental agencies regarding the desirability of maintaining medical education, internships and hospital residencies throughout any emergency.

FUNCTIONS OF THE COMMITTEE

After extended discussion of the organization within the individual states and counties, a subcommittee was appointed to prepare an outline of the functions of the members of the National Committee on Medical Preparedness and of the chairmen of the state committees. This was published in THE JOURNAL last week.

THE EXECUTIVE COMMITTEE

In view of the death of Dr. Austin A. Hayden, who was a member of the Executive Committee of the Committee on Medical Preparedness of the American Medical Association, Dr. Irvin Abell was elected to the Executive Committee to replace him. The other members are Drs. Olin West and Morris Fishbein.

ESSENTIAL TEACHERS

In order to aid the continuation of medical teaching, it was decided to request the executive committee of each of the medical schools of the United States to send to the Committee on Medical Preparedness a list of the personnel essential for teaching the student body of the size now existing.

EDUCATION THROUGH MEDICAL SOCIETIES

Plans were also made for each medical society throughout the nation to develop contact with representatives of the Army and Navy Medical Departments and the United States Public Health Service, with a view to arranging programs of education for civilian practitioners regarding the fundamentals of enrolment in such services.

It was urged also that members of the Committee on Medical Preparedness be available to medical organizations for addresses regarding functions of the Committee.

A procedure was adopted for calling the Committee on Medical Preparedness into special session and also for a meeting in the headquarters office of the American Medical Association of the state chairmen.

PLANS FOR CONSCRIPTION

Information was developed indicating that the setting up of a plan of conscription would involve a number of local draft boards in the individual states, with the sending of the men for examination to perhaps 100 different localities established throughout the United States for final military examination. In each of these hundred localities approximately eleven physicians would be required—men qualified in the medical specialties—to make final examinations so that individuals unfit for service would not be sent to camp, the idea being to have the examination as near as possible to his home and thus to disrupt his economic relationships as little as possible. Attention was called particularly to the need of specialized service for the examination of x-ray films of the chest for the detection of tuberculosis.

ENROLMENT OF VOLUNTARY BLOOD DONORS

The American Red Cross, acting at the request of the Surgeon General of the United States Army, has announced plans for the promotion of a nationwide corps of volunteer blood donors which would become part of the national defense program, when and if needed.

For the past four years twelve Red Cross chapters have been furnishing whole blood from volunteers to hospitals for civilian use. The new program will be patterned along similar lines, using plasma instead of whole blood.

A preliminary study involving 1,300 Red Cross volunteers in four cities throughout the country will be conducted under the direction of a special committee appointed by the National Research Council, including Dr. Cyrus E. Sturgis of the University of Michigan, Dr. Everett Plass of the University of Iowa, Dr. Alfred Blalock of Vanderbilt University and Dr. Max Strumia of Bryn Mawr Hospital, Philadelphia.

Dr. William DeKleine, medical director of the Red Cross, has said that the proposed plan for collecting blood is patterned after the blood bank idea except that plasma will be used instead of whole blood. Preliminary studies will be made to perfect methods of collecting, storing and administering plasma under conditions comparable to war-time emergency. Blood for this initial study will be furnished by volunteers at the various hospitals where members of the Research Committee are regularly employed. The plasma collected will be stored and used as emergencies arise at these hospitals.

After these preliminary investigations have been completed, the Red Cross will then work out with the medical department of the army plans for enrolling prospective donors in cities throughout the country where collecting centers will be established. Blood so collected will be pooled in large sterile containers, to simplify storage, in sufficient quantities to meet the emergency needs for treating the wounded.

Recruiting donors will be conducted by a special chapter blood transfusion committee which will include leading local physicians. The technical phases of the project will be performed by the medical staff of the cooperating hospitals. They will examine the prospective volunteers and make the necessary blood tests as well as doing the actual transfusions.

Plague in the United States.—From the time of the first appearance of plague in the United States in 1900 to Jan. 1, 1940, there have been recorded 499 cases with 314 deaths. These figures may not agree with those presented elsewhere, as they have been compiled from various sources; and it may be reasonable to assume that, because of conditions existing in the Chinese quarter of San Francisco during the first plague epidemic in that city, and other difficulties which hampered the work of investigation and control, a complete record of cases in Chinese was not secured. Human cases of the disease in the United States have been reported in eight states, in chronological order of first appearance as follows: California, 1900; Washington, 1907; Louisiana, 1914; Florida, 1920; Texas, 1920; Oregon, 1934; Utah, 1936; Nevada, 1937. The last human case of plague in the United States, up to Jan. 1, 1940, was reported in Millard County, Utah, on Dec. 4, 1939.—Hampton, Brock C.: Plague in the United States, *Pub. Health Rep.* **55**:1143 (June 28) 1940.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Seven Cases of Poliomyelitis.—Seven cases of poliomyelitis were reported in Houston County, near Webb, July 17, according to newspaper accounts.

Changes in Health Officers.—Dr. Otis F. Gay, Ashland, head of the health unit in Clay County, has been appointed to a similar position in Butler County, succeeding Dr. William M. Askew Jr., Greenville, who resigned to enter private practice. Dr. David B. Snelling, Butler, health officer of Choctaw County, has been appointed in charge of the unit in Greene County, with headquarters in Eutaw. Dr. W. D. Burkhalter, Montgomery, will be acting health officer in Choctaw County until a permanent appointment has been made. Dr. Rutherford O. Ingham, Montgomery, has been appointed health officer of Henry County, with headquarters in Abbeville.

CALIFORNIA

Changes in Faculty.—The University of California Medical School, San Francisco, announces that the title "dean emeritus" has been given to Dr. Langley Porter. Dr. Porter retired this year. In 1936 he first retired from the deanship, to which he had been appointed in 1927, but following the death of Dr. Williams McKim Marriott, who died shortly after taking over the position, Dr. Porter again assumed the office. He has been associated with the school since 1918. His successor has not yet been named. Appointments announced at the school recently include Drs. Douglas G. Campbell as assistant clinical professor of psychiatry and Hubert R. Hathaway as assistant professor of anesthesia.

Courses for Practicing Physicians.—Postgraduate courses for practicing physicians will be conducted by Stanford University School of Medicine in cooperation with the San Francisco Department of Public Health and the San Francisco Hospital, San Francisco, September 9-13. Registration will close August 31. The fee will be $25. The courses will cover pediatrics, gastro-enterology, surgical anatomy and operative technic, management of hypertension and nephritis, x-ray diagnosis and therapy, proctology, surgical emergencies, traumatic injuries and fractures, otorhinolaryngology and anesthesiology. In addition, general meetings will be held in the evenings with the following speakers: Drs. Windsor C. Cutting, Lowell A. Rantz and Arthur P. Richardson on "Chemical Warfare Against Bacterial Disease"; George S. Johnson, "Emotions at War" and Arthur L. Bloomfield, William Dock and David D. Mason, who will conduct a clinicopathologic conference. All fees are payable to the school of medicine; checks and applications should be mailed to the dean, 2398 Sacramento Street, San Francisco, not later than August 31.

Psittacosis Traced to Los Angeles Birds.—The California state department of health has traced a fatal case of psittacosis in Caldwell, Idaho, and three cases in Tucson, Ariz., to a Los Angeles pet shop, according to *Public Health Reports*, June 7. The Idaho case occurred in December 1939 in a person who had bought a pair of parakeets in November from a local dealer. The parakeets had been purchased early in November from the Los Angeles shop, and psittacosis was subsequently proved in all the birds in that lot as well as in other birds in the Los Angeles stock. No infection was found in the California aviaries that supplied the Los Angeles dealer, but as he had imported birds from other countries it seemed probable that the infection was introduced by the imported birds, according to the report. The Arizona cases occurred in a family which owned birds purchased in the same Los Angeles shop. When psittacosis was suggested the birds were set free and were therefore not available for examination. The patients were two young adults in the same family and a nurse who cared for them.

DELAWARE

Executive Secretary of Board.—Dr. Edwin Cameron, Morgantown, W. Va., director of the Monongalia County Health Department, has been appointed executive secretary of the Delaware State Board of Health, according to the *American Journal of Public Health*. The appointment was effective July 1. Dr. Cameron graduated at Dalhousie University Faculty of Medicine, Halifax, N. S., in 1927.

FLORIDA

Changes in Health Officers.—Dr. Leland H. Dame, West Palm Beach, has been appointed director of the Hamilton County health unit.——Dr. Irving E. Simmons, Quincy, has resigned as health officer of Gadsden County to become head of the new unit in Nassau County. Dr. Samuel J. Ravitch, Peekskill, N. Y., is acting director in Gadsden County.

Sectional Meeting on Surgery.—The Florida section of the Southeastern Surgical Congress will hold its seventh annual clinical conference at the Jackson Memorial Hospital, Dade City, August 31. Included on the program will be:

Dr. Robert L. Sanders, Memphis, Tenn., Complications of Peptic Ulcer.
Dr. William G. Hamm, Atlanta, Ga., Skin Grafting.
Dr. Thomas C. Davison, Atlanta, Breast Tumors.
Dr. Herbert Acuff, Knoxville, Tenn., Surgical Phases of Lung Abscess.
Dr. Edward Jelks, Jacksonville, Carcinoma of the Stomach.
Dr. Louie M. Limbaugh, Jacksonville, Medical Care of the "Surgical" Diabetic.
Dr. Benjamin T. Beasley, Atlanta, Uterine Displacements with Demonstration of an Original Apparatus Designed to Treat These Conditions.

GEORGIA

Gift for Library.—A grant of $10,000 has been allowed by the Rockefeller Foundation to purchase books and journals for the library of the University of Georgia School of Medicine, Augusta, according to the state medical journal. The grant will supplement the Moore Fund, given to the school by Mrs. Julia Carter Moore, Augusta.

Rabies Among Foxes.—The state department of health reports in its July bulletin an outbreak of rabies among foxes in three counties. During the past month, it stated, the heads of five foxes were received for examination. Two were too badly decomposed for examination, but three showed positive evidence of rabies. Foxes have also been found dead in one county without having external signs of the cause of death. A number of foxes attacking human beings and domestic stock have been reported. The counties involved are Burke, Jefferson and Jenkins. In March a hunting dog went rabid and while in the early stages bit several foxes, which escaped. About a month later a rabid fox was killed in the vicinity and several mules bitten by foxes later developed rabies. The reports on foxes attacking human beings, domestic stock and hunting dogs have been coming in constantly since that time. A plan is under way to investigate the outbreak under the cooperation of the Burke County board of health, the state department of health, the state wild life department, the federal biologic survey and the Rabies Research Laboratory of the Rockefeller Foundation.

INDIANA

Personal.—Dr. Aaron M. Winklepleck, assistant to the superintendent of the Indiana State Sanatorium at Rockville, has been appointed head of the Smith-Esteb Memorial Hospital, Richmond. He succeeds Dr. Robert A. Staff, who was recently named superintendent of the Indiana State Sanatorium.——Dr. and Mrs. Byron W. Marshall, Gary, were guests of honor at a farewell dinner recently given by neighbors, patients and friends on the occasion of Dr. Marshall's retirement from active practice and the couple's departure from Gary. Dr. George W. Gannon presented Dr. Marshall with an oil painting of a scene in Brown County, of which Dr. Marshall is a native and where he and Mrs. Marshall plan to live.

District Meeting.—The Eighth District Medical Society met in Elwood, June 19, and presented the following program:

Dr. Guy A. Owsley, Hartford City, Borderline Allergy in General Practice.
Dr. Bruce W. Stocking, Muncie, X-Ray Diagnosis in Abdominal Diseases.
Dr. George C. Stevens, Indianapolis, Mental Hygiene Clinic and the Physician.
Dr. Edwin Rogers Smith, Indianapolis, Use of Metrazol in Certain Mental Diseases.
Dr. John C. Drake, Anderson, Recent Advances in Treatment of Fractures of the Hip.
Dr. Willis D. Gatch, Indianapolis, Cause and Treatment of the Symptoms of Peritonitis.

Albert Stump, Indianapolis, counsel for the Indiana State Medical Association, addressed the dinner session on "Legal Problems in Care of Indigents."

IOWA

Health Exhibit at State Fair.—The Iowa State Department of Health will conduct an exhibit at the state fair, August 21-30, featuring the public health nurse and her work in connection with infant and child health.

Society News.—Dr. Harold Dabney Kerr, Iowa City, discussed "The Present Status of Radiotherapy" before a combined meeting of the Bremer County Medical Society and the

staff of Mercy Hospital in Waverly recently.——Dr. John H. Matheson, Des Moines, addressed the Hardin County Medical Society in Iowa Falls, June 25, on common diseases of the eye.——At a meeting of the Jackson County Medical Society in Bellevue, June 27, Drs. Horace M. Korns and Willis M. Fowler, Iowa City, spoke on "Diagnosis and Treatment of Cardiac Arrhythmias" and "Modern Treatment of Anemias."

KANSAS

Personal.—The staff of St. Margaret's Hospital, Kansas City, gave a dinner recently in honor of Drs. Richard C. Lowman, Kansas City, and Owen W. Krueger, Kansas City, Mo., celebrating their completion of fifty years in the practice of medicine. Dr. George M. Gray, Kansas City, treasurer of the state medical society, was also a guest and Dr. John F. Hassig, Kansas City, was the toastmaster.——Dr. Thomas L. Foster has been appointed superintendent of the Osawatomie State Hospital, effective June 1; he has been assistant superintendent of the Larned State Hospital for the past eight years.

MICHIGAN

Tuberculosis in Michigan.—Tuberculosis deaths for the whole state in 1939 held close to the record low of 1938, but rates of individual counties varied widely, according to a release from the state department of health. Deaths from tuberculosis in the state totaled 1,881 in 1939, showing a rate of 36.9 deaths per hundred thousand of population as compared with 1,866 deaths and a rate of 36.6 in 1938. Detroit had 945 of the 1,881 deaths in 1939. Crawford and Oscoda counties were free from tuberculosis deaths for the second consecutive year, and a third county reporting no deaths was Gladwin.

Changes in Health Officers.—Dr. Frank J. Hill, Waterbury, Conn., was recently named health officer of the Mason-Manistee health unit.——Dr. Clifton F. Hall, Big Rapids, has been appointed director of the Mecosta-Osceola health department; he has been acting director since October 1939.——Dr. Roelof Lanting, who, during a leave of absence as director of the Delta County health department, Escanaba, has been studying in the graduate school of public health and hygiene, University of Michigan, Ann Arbor, has been appointed director of health district number 7 with headquarters in Gladwin. Dr. Fred O. Tonney, formerly of Chicago, acting director of the Delta County unit, will remain there until a new director has been named before accepting a recent appointment to the staff of the state department of health at Lansing, newspapers reported.——Dr. Jacques P. Gray, Berkeley, Calif., has been appointed director of the Hillsdale County health department. In this capacity he will be a representative of the W. K. Kellogg Foundation in Hillsdale County, a unit of the Michigan Community Health Project.——Dr. Erwin F. Hoffman, Iron Mountain, has resigned as health officer of Dickinson County to join the Florida state department of health, Jacksonville.

MINNESOTA

Supreme Court Upholds Suspension of License.—The Supreme Court of Minnesota, May 17, in a unanimous opinion affirmed a ruling of the district court of Ramsey County that the order of the Minnesota State Board of Medical Examiners suspending the license of Dr. Gottfried Schmidt, Lake City, for five years "was neither arbitrary, oppressive nor unreasonable." The license was suspended by the state board, Dec. 16, 1938, following a complaint made by a former patient to the board. According to a report from the state board, the hearing brought out that Dr. Schmidt attempted to diagnose cancer, brain tumor, stomach ulcer and other serious ailments by having the patient moisten a piece of wood pulp paper with saliva and then placing the paper on the abdomen of the patient or on the abdomen of a woman employed by Dr. Schmidt in his office in Lake City. He also claimed that he had a machine with which he could broadcast treatments to absent patients. Dr. Schmidt was twice warned by the state medical board to desist from such practices. Justice Stone's opinion described Dr. Schmidt's diagnostic methods as "so clearly bald quackery, and so much an imposition on his patients, that the testimony of three patients with whom he had good luck would not have helped him." Dr. Schmidt was born in Minnesota in 1871 and graduated at the University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, in 1903. He had practiced in Lake City for twenty years, it was stated.

NEW YORK

Society News.—Dr. L. Whittington Gorham, Albany, addressed the semiannual meeting of the Montgomery County Medical Society, June 18, at Fort Plain, on "Differential Diagnosis of Coronary Occlusion."——Dr. Richard Nauen, Ray Brook, discussed diagnosis of tuberculosis at the semiannual meeting of the Medical Society of the County of Essex, June 4.——Drs. Ray D. Champlin, Oneonta, and John C. McClintock, Albany, addressed the Otsego County Medical Society, Oneonta, June 19, on "The Doctor in War Time" and "Preventing Complications of Thyroid Gland Disease" respectively.——At the semiannual meeting of the Steuben County Medical Society at the Veterans Administration Facility in Bath, June 13, the speakers were Drs. Heyward H. Hopkins, Rochester, on "The Vallium Cup"; Sidney N. Eichenholtz and Abraham Falk of the facility staff on "Low Back Pains" and "Undulant Fever" respectively.

New York City

Bequests to Hospitals.—Several hospitals and other institutions received large bequests from the estate of the late Mrs. Marie Engert-Colman, who died in England recently. Among the bequests are the following: St. Peter's, St. Catherine's, Brooklyn, Wyckoff Heights, Long Island College hospitals, Brooklyn, and Mary Immaculate Hospital, Jamaica, and St. Vincent's Hospital, New York, $30,000 each; St. Mary's Hospital, $50,000 and the proceeds from the sale of jewelry; Faith Home for Incurables, Visiting Nurse Association of Brooklyn, House of St. Giles the Cripple, Brooklyn Home for Consumptives, $25,000 each.

Faculty Changes at Columbia.—Dr. Alphonse Raymond Dochez, John E. Borne professor of medical and surgical research, Columbia University College of Physicians and Surgeons, has been appointed executive officer of the department of bacteriology, according to *New York Medical Week*. Dr. Dochez succeeds the late Dr. Frederick P. Gay. Dr. LeGrand H. Hardy has been made assistant clinical professor of ophthalmology and Dr. Solomon Biloon promoted to assistant clinical professor of medicine. Mary Swartz Rose, Ph.D., professor of nutrition, will retire July 1, 1941, after a year's leave of absence. Dr. Rose is a member of the Council on Foods and Nutrition of the American Medical Association.

Dysentery on Refugee Ship.—Thirty-six cases of a mild bacillary dysentery were found on the *S. S. Washington* when she arrived from Galway, Ireland, July 13, bringing Americans from the war zones. The illness was limited to the tourist class, in which there were 829 passengers. When inspectors from the health department reached the boat seven who apparently recovered had disembarked, but twenty-nine who were still ill remained aboard. As these recovered at intervals they were allowed to disembark, but seven were still aboard July 15, according to *New York Medical Week*. The health department followed up all passengers living in New York and notified state health departments concerning those who lived elsewhere. An epidemiologic investigation was being made.

NORTH CAROLINA

Society News.—Dr. Frank Wood, Marion, among others, addressed the Thermal Belt Medical Society, Saluda, July 11, on "Prophylactic Use of Sulfanilamide."——At a meeting of the Catawba Valley Medical Society, July 11, the speakers were Drs. Frank W. Jones, Newton, on "Management of Some Chest Injuries"; Franklin C. Smith, Charlotte, "Fallacies in Ophthalmology," and John W. Ervin, Morganton, who reported a case of thrombopenia with leukemia of unknown origin.——Mr. John Elliott, Salisbury, addressed the Forsyth County Medical Society, Winston-Salem, June 18, on "The Use of Plasma as a Substitute for Whole Blood."——Dr. Samuel F. Ravenel, Greensboro, addressed the Buncombe County Medical Society, Asheville, July 15, on "Complications of Acute Hemorrhagic Nephritis in Children." Dr. Samuel M. Bittinger, Black Mountain, was the speaker July 1 on "Nontuberculous Diseases of the Lung."

Personal.—Dr. Wingate M. Johnson, Winston-Salem, received the honorary degree of doctor of science at the recent commencement at Wake Forest College.——Dr. William L. Patman, Greensboro, has been appointed general director of Chatham Hospital, Siler City.——Dr. Wilfred N. Sisk, recently on the staff of the Venereal Disease Medical Center, U. S. Public Health Service, Hot Springs National Park, Ark., has been appointed health officer of Buncombe County to succeed the late Dr. Howard L. Sumner.——Dr. Robert L. Russell, chief of the tuberculosis and general medical service at the Veterans Administration Facility, Oteen, retired from the service recently, it is reported. He will reach the age limit in

September.——Charles D. Van Cleave, Ph.D., formerly instructor of anatomy, Cornell University Medical School, has been appointed assistant professor of anatomy at the University of North Carolina School of Medicine, Chapel Hill.

OHIO

New State Laboratory.—The state emergency board has set aside $50,000 for a new laboratory building for the state department of health in Columbus. It will be erected on the campus of Ohio State University and marks another step toward the goal of state and university officials to concentrate all health department facilities on the campus. According to the state medical journal, the project calls for a $350,000 building, of which the new laboratory structure will be one wing, but construction of the whole unit must await legislative appropriation. At present most of the health department's laboratory facilities are in an old building on the campus, which will be dismantled after their removal. Because of lack of space the laboratories for the division of industrial hygiene are now in a rented office building in downtown Columbus. All offices of the health department except the laboratories are now located on the third floor and in the basement of the State Office Building.

PENNSYLVANIA

Personal.—Dr. Everett S. Barr has resigned as medical director of the Chester County Hospital, West Chester, it is reported.——Dr. Ralph Lee Hill, medical superintendent of the Wernersville State Hospital, received the honorary degree of doctor of science at the recent commencement of Franklin and Marshall College, Lancaster.

Society News.—Dr. Paul A. Keeney, Harrisburg, was named president-elect of the Pennsylvania Public Health Association at the recent annual meeting and Mr. Harold H. Keller, Philadelphia, became president. Dr. John J. Shaw, state secretary of health, Harrisburg, is honorary president.——Dr. Joseph H. Barach, Pittsburgh, addressed the Warren County Medical Society, Warren, July 8, on "The High Carbohydrate Diet and Newer Insulins in the Treatment of Diabetes."——Dr. Charles B. Daugherty, Tyrone, addressed the Blair County Medical Society, June 25, in Altoona on national mobilization and defense.——Dr. Carl E. Ervin, Harrisburg, addressed the Medical Society of Franklin County, June 18, on "Disorders of the Thyroid."

Philadelphia

Dr. Riesman's Bequests.—Dr. David Riesman, who died June 3, ordered in his will that his brain be given to the Wistar Institute of Anatomy for research purposes, according to a newspaper report. Among several charitable bequests were $1,000 to the College of Physicians of Philadelphia; $500 to the Philadelphia County Medical Society and $2,000 to the medical board of the Philadelphia General Hospital "to encourage research on the part of the staff—not a prize but a stipend."

The Bicentennial Conference.—The University of Pennsylvania will hold a conference on medical, natural and social sciences, fine arts, humanities and religion, September 16-20, as part of the observance of the two hundredth anniversary of the founding of the university. The program on the medical sciences will consist of one address each morning, followed by symposiums. Those who will give the addresses, according to the preliminary program, are:

Dr. Thorvald Madsen, director of the State Serum Institute, Copenhagen, Denmark, subject to be announced.
Dr. Lawrence J. Henderson, Abbott and James professor of chemistry, Harvard Medical School, Boston, The Study of Man.
Dr. Evarts A. Graham, Bixby professor of surgery, Washington University School of Medicine, St. Louis, Two Centuries of Surgery.
William Mansfield Clark, Sc.D., De Lamar professor of physiological chemistry and director, department of physiological chemistry, Johns Hopkins University, Baltimore, A Challenge to Scholarship.

The symposiums will cover the following topics: problems and trends in virus research, therapeutic advances in psychiatry, medical problems of old age, nutrition, female sex hormones, hypertension, genesis of cancer, dental caries, development of occlusion, problems of intestinal obstruction, the relation of diseases in lower animals to human welfare, modern aspects of the antituberculosis program, chemotherapy, the university and public health statesmanship. More than fifty speakers will take part in these discussions. On Friday, September 20, there will be an alumni meeting, followed by a special convocation to be attended and addressed by the President of the United States. On Saturday, September 21, officials of the university will hold a reception for official delegates to the conference, and this will be followed by the bicentennial convocation, at which honorary degrees will be conferred on a group of scholars. Inquiries about any of the proceedings during the Bicentennial Celebration should be addressed to the Registrar of the Bicentennial Conference, University of Pennsylvania, Philadelphia.

TENNESSEE

Society News.—The Dyer, Lake and Crockett Counties Medical Society, Dyersburg, was addressed recently by the following Memphis physicians: Drs. Harwell Wilson, diagnosis and management of thyroid disease; Robert L. Sanders, dyspepsia; Robert Lyle Motley, hypertension; Raphael Eustace Semmes, surgical aspects of hypertension, and Thomas D. Moore, renal aspects of hypertension.——Dr. William H. Enneis addressed the Knox County Medical Society, Knoxville, recently on undulant fever.——Drs. Joseph H. Francis and Joseph A. Crisler, Memphis, addressed the Madison County Medical Society recently on "Treatment of Duodenal Ulcer" and "Management of Various Types of Goiter" respectively.——Speakers at a meeting of the Washington County Medical Society recently were Drs. Horace B. Cupp, Mountain Home, on "Spinal Anesthesia"; Wallace L. Poole, Johnson City, and Carroll H. Long, New Orleans, "Use of Pentothal Sodium as an Intravenous Anesthetic."

UTAH

State Medical Meeting in Ogden.—The annual meeting of the Utah State Medical Association will be held in Ogden, August 29-31, with the Weber County Medical Society celebrating its fiftieth anniversary as a special feature. The program includes the following guest speakers:

Dr. James Dewey Bisgard, Omaha: Treatment of Carcinoma of the Bowel; Recent Advances in Surgery.
Dr. James G. Carr, Chicago: Obscure Fever; Clinical Diagnosis of Coronary Occlusion.
Dr. James F. Churchill, San Diego: Diagnosis and Management of Heart Irregularities; Congestive Heart Failure.
Dr. Herbert E. Coe, Seattle: Congenital Defects—A General Survey and Prognosis; The Bearing of Growth and Development on Children's Surgery.
Dr. Fred J. Hodges, Ann Arbor, Mich.: Titles to be announced.
Dr. Verne C. Hunt, Los Angeles: Surgical Significance of Gastrointestinal Bleeding; Obstructing Lesions of the Common Duct.
Dr. Joseph E. J. King, New York: Oxycephaly; Brain Abscess.
Dr. Paul B. Magnuson, Chicago: Fractures of the Neck of the Femur, Both Recent and Ununited; Relief of Certain Types of Arthritis by Surgery.
Dr. James T. Priestley, Rochester, Minn.: Conservative Surgical Treatment of Staghorn Renal Calculi; Carcinoma of the Bladder with Particular Reference to Total Cystectomy.
Dr. John E. Raaf, Portland, Ore.: Diagnosis and Treatment of Late Effects of Head Injuries; Treatment of Patients with Protruded Intervertebral Disks.

WISCONSIN

Society News.—Dr. Henry L. Greene, Madison, addressed the Jefferson County Medical Society, June 20, in Jefferson on "Epiphyseal Injuries in Children."——Dr. Sumner L. S. Koch, Chicago, addressed the Brown-Kewaunee-Door Counties Medical Society, Green Bay, June 11, on "Injuries, Infections and Deformities of the Hand."——Drs. Hugh F. Ringo and Mark W. Garry, Montreal, addressed the Ashland-Bayfield-Iron Counties Medical Society, June 26, in Ironwood on prevention of silicosis in iron miners.——Speakers before the Trempealeau-Jackson-Buffalo Counties Medical Society in Galesville, July 18, were Drs. Walter G. Sexton and Lyman A. Copps, Marshfield, on "Hematuria" and "Interesting Eye Conditions" respectively.

GENERAL

Missing Physician Found.—Dr. Runyon H. Irvin, Mount Vernon, Ill., reported recently to be missing from home, was found in a hospital in Newark, N. J. He had been injured when a heavy sliding door struck him. Identification was established through an announcement of Dr. Irvin's disappearance in THE JOURNAL, July 27, page 312.

Board of Anesthesiology Increases Fees.—The American Board of Anesthesiology announces that on account of increased administrative expenses it has been necessary to increase the application and administrative fees. The new fees are $25 with application and $50 before examination. In case of rejection, all fees paid will be refunded except a $10 filing fee (before full examination). These new fees go into effect Jan. 1, 1941. If application is filed before that time, the rate of $50 ($5 for registration, not returnable, and $45 examination fee) still applies. Dr. Paul M. Wood, 745 Fifth Avenue, room 1503, New York, is secretary.

Opening for Superintendent of Hospitals.—The Civil Service Commission, Minneapolis, announces an opening for the position of superintendent of hospitals. Applications may be

obtained from the commission at room 109, City Hall, Minneapolis. The examination will be open to citizens of the United States who have been residents of the United States for at least one year immediately preceding the date of closing of applications, September 11. Candidates must not have reached their fifty-fifth birthday and must be graduates of a recognized medical school with at least ten years of successful experience as a physician, surgeon or medical executive. This experience shall include five years as an administrator or superintendent in an accredited hospital of a capacity of at least fifty beds, or three years as an administrator, superintendent or assistant superintendent in an accredited hospital with a bed capacity of at least 200, or one year in these positions in an accredited hospital with at least a 500 bed capacity. The salary will be $5,000 annually with living quarters or $6,000 without quarters.

Clinic on Health in Industry.—The Muskegon Employers Association, the Employers Association of Grand Rapids and the National Association of Manufacturers sponsored a clinic on health in industry at the Occidental Hotel, Muskegon, Mich., June 28. The program included:

The Meaning and Value of Industrial Health, as analyzed by the state health department, Dr. Kenneth E. Markuson, Lansing, director, Michigan Bureau of Industrial Hygiene; as evaluated by the state medical society, Dr. Henry Cook, Flint, chairman, Michigan Committee on Occupational Disease and Industrial Hygiene; as experienced by the manufacturer, Mr. H. M. Taliaferro, president, American Seating Company.

Organization and Costs of an Industrial Health Service, Dr. Constant M. Colignon, Muskegon, Mich., medical director, Campbell, Wyant and Cannon Foundry Company.

A Plant Health Program and Public Relations, Mr. Ralph L. Lee, department of public relations, General Motors Corporation.

Dr. Victor G. Heiser, New York, consultant, committee on healthful working conditions, National Association of Manufacturers, addressed a luncheon session on "Industrial Health and National Defense."

Society News.—Dr. Fred H. Albee, New York, was elected president of the International College of Surgeons at a meeting in Philadelphia in June. The United States chapter and the governing council decided to transfer headquarters of the organization from Geneva to Washington for the duration of the war. Dr. Desiderio A. Roman, Philadelphia, was elected president of the United States chapter.——Dr. Matthew C. Riddle, Portland, Ore., was named president-elect of the Pacific Northwest Medical Association at its annual meeting in Spokane, Wash., July 12, and Dr. Donald A. Palmer, Spokane, was installed as president. State councilors were elected as follows: Drs. Orval F. Swindell and Everett N. Jones, Boise, Idaho; Arthur J. Movius, Billings, Mont.; Howard P. Kirtley and Emerson F. Root, Salt Lake City, Utah; Doyle Joslin, Rock Springs, and Herbert L. Harvey, Casper, Wyo. The next meeting also will be held in Spokane.——Col. Harold W. Jones, librarian of the Army Medical Library, Washington, D. C., was reelected president of the Medical Library Association at its annual meeting in Portland, Ore., June 25-27. Dr. Robert E. Schlueter, St. Louis, was elected vice president and Miss Anna C. Holt, Harvard Medical School Library, Boston, was reelected secretary. The 1941 convention will be held at the University of Michigan Medical School, Ann Arbor.

Fatal Accidents.—The U. S. Bureau of the Census recently released a statistical study of fatal accidents in the six years 1933 to 1938. The report shows that in 1933 fatalities from accidents totaled 90,932 and thereafter the number increased to a high point of 110,052 in 1936. Then it decreased to 93,805 for 1938. Special emphasis was placed on deaths caused by fires, which ranked seventh among all accidental causes from 1933 to 1938 and advanced to sixth place in 1938. Figures for the years in succession were 1,521 in 1933, 1,752 in 1934, 1,581 in 1935, 1,913 in 1936, 1,688 in 1937 and 1,650 in 1938. Fire claimed more victims in the age group 5 to 9 than in any other group in 1938; there were 129 deaths in this group, which was 7.8 per cent of all persons burned to death. The next largest number was in the group 50 to 54, with 109 deaths. Age distributions for different types of fatal accidents vary greatly, the report showed. Only 18.3 per cent of deaths from injury by fall occurred among persons under 45 years old, who constitute 77 per cent of the population; but 55.8 per cent of the automobile fatalities and 91.3 per cent of the air transportation accidents were in this younger group. The report includes several tables indicating the accident fatalities for individual states and for cities with a population of 100,000 or more. It tabulates for all types of accidents the number of deaths, the death rate per hundred thousand of estimated population, the percentage of all deaths from accidents and the rank-order frequency among the different types of accidents.

LATIN AMERICA

Society News.—The Second National Medical Congress in Peru is to be held this month in Arequipa under the auspices of the Peruvian government in connection with the celebration of the four hundredth anniversary of the founding of the city. There will be four sections: medicine, surgery, hygiene and social medicine, and specialties.——The First Cuban Congress of Regional Pathology, Social Medicine, Preventive Medicine, Public and Private Hygiene was recently held with Dr. Juan de Moya Flamand, secretary of health and welfare, as president. The congress studied problems relating to the diseases peculiar to Cuba in connection with environments of each region, methods of eradicating them and methods of disseminating information on hygiene and sanitation.——Dr. Ramon Castroviejo, New York, addressed the Society of Ophthalmology of São Paulo, Brazil, recently on "Surgery of the Cornea." He was also honored by a banquet given by the society.

FOREIGN

Prize Offered for Essay in Ophthalmology.—The Ophthalmological Society of the United Kingdom announces the Treacher Collins Prize, which is awarded triennially for the best essay on a subject chosen by the council of the society. The prize is open to qualified medical practitioners of any nationality but must be written in English. The subject is "Allergy of the Eye and Its Adnexa." Essays should be submitted before December 31 to the honorary secretary, Ophthalmological Society of the United Kingdom, 5 Racquet Court, Fleet Street, London, E. C. 4. Names should not be on the essay but a distinguishing pseudonym or quotation, which should also be on a sealed envelop containing the candidate's name and address to accompany the essay.

CORRECTIONS

Sarcoidosis.—The first bibliographic reference in the editorial "Sarcoidosis" in THE JOURNAL, July 27, should read the *New England Journal of Medicine* instead of the *British Journal of Dermatology*.

Morphine Derivative in Massive Doses.—In THE JOURNAL, July 20, page 259, there appeared an abstract entitled Morphine Derivative in Massive Doses. The drug in question, known as Eupaverine, is 1-(3,4-methyl-enedioxybenzyl)-3-methyl-6,7-methylenedioxyisoquinoline and should be properly classified in the isoquinoline group of drugs obtainable from opium. The actions of members of this group of compounds differ in many respects from the phenanthrene group of drugs also obtainable from opium. It is the latter group which contains morphine and its derivatives.

Government Services

The Government Needs Physicians

The U. S. Civil Service Commission announces open competitive examinations to fill medical officer positions in the U. S. Public Health Service and the Food and Drug Administration, Federal Security Agency; Veterans' Administration; Civil Aeronautics Authority, Department of Commerce, and the Indian Service, Department of the Interior. The examinations cover three grades with salaries ranging from $3,200 to $4,600, subject to a deduction of 3.5 per cent toward a retirement annuity. Applications must be filed with the civil service commission, Washington, D. C., and will be received until further notice. Applicants must have graduated with an M.D. degree from a recognized medical school and must have had professional experience in one of the following optional branches: aviation medicine; cancer research; cardiology; dermatology; eye, ear, nose and throat (singly or combined); general practice; industrial medicine; internal medicine and diagnosis; medical pharmacology; neuropsychiatry; pathology, bacteriology and roentgenology (singly or combined); public health; surgery; tuberculosis, and urology. For some positions in the Veterans' Administration, applicants for associate medical officer need not have had experience other than one year of internship. Applicants for the associate grade must not have passed their fortieth birthday, and for the other two grades they must not have passed their fifty-third birthday. Announcements containing further information and the application forms may be obtained from the secretary of the board of U. S. Civil Service Examiners at any first or second class postoffice or from the U. S. Civil Service Commission, Washington, D. C.

Foreign Letters

LONDON

(From Our Regular Correspondent)

July 6, 1940.

The Evacuation of Dunkirk

The Emergency Hospital Service was established for dealing with the heavy casualties expected from air raids among the civilian population. The London area was divided into ten sectors, each with its apex in central London near one of the large hospitals (which would act as a casualty clearing station) and widening out to advanced bases and then to base hospitals 30 or 40 miles away, so as to be safer from bombing. No casualties have yet occurred in London, but the scheme has been put to its first test on a large scale by an emergency in which the stream of casualties came in the opposite direction to the expected one. In the days preceding the evacuation of Dunkirk 7,000 beds were made ready. From the hospital ships the most serious cases were taken to hospitals near the ports; the less severely wounded were sent by train to hospitals farther away. After the hospital ships came the smaller boats, each having some wounded to disembark. It was not known when the flow would stop and so arrangements were made to evacuate many of the less seriously wounded to hospitals still farther off in the west, with the result that the sector in use could comfortably have dealt with three times the number of casualties it was called on to handle. Actually 1,873 cases were treated in the sector hospitals in a period of twelve days. These included French, Belgian and British soldiers and sailors and a few refugees. Although nearly half had received no treatment other than first aid and were carried in ambulances from 30 to 60 miles, only thirty-three (1.7 per cent) died. The response of the sector hospitals was wonderful. Not one was found to confess that it could not undertake more work. Every one made it a point of honor to see that everything possible was done for the incoming wounded with the maximum of speed. As the work increased, mobile surgical teams were sent from London and additional trained operating room nurses, house officers and student dressers were drafted into coastal towns that needed help.

Sulfathiazole in Staphylococcic Infections

At a meeting of the Section of Therapeutics and Pharmacology a discussion took place on the use of sulfathiazole, particularly in staphylococcic infections. Mr. E. C. Butler said that staphylococcic septicemia was much more common and fatal than was generally supposed. Every death from osteomyelitis and nearly every death from cavernous sinus thrombosis and many deaths from boils, carbuncles and infected fingers could be attributed to Staphylococcus aureus. Any treatment to be effective must be started at the beginning of the disease. At the London Hospital every patient with a severe staphylococcic infection was given 20,000 units of antitoxin. It was also necessary to find a drug which may help to destroy staphylococci. The sulfonamides did not affect the course of the severe cases. Staphylococcic infections were far more difficult to treat than hemolytic streptococcus infection. He had found sulfathiazole of little or no effect on a staphylococcic infection when the blood culture was positive. But it might be of benefit after the source of the bacteria had been removed or when the lesion was localized, as in carbuncle or cellulitis. But it must be given early, and surgical treatment and antitoxin must not be neglected. The results so far did not support the optimistic reports from America.

Dr. George Melton reported five cases of osteomyelitis and five of carbuncle of the face treated with sulfathiazole. The first case, an acute osteomyelitis of the radius and ulna after open reduction of a fracture, improved but did not clear up under sulfapyridine. Sulfathiazole was then given to a total dosage of 26 Gm. After each injection the patient complained of headache and vomited, but marked improvement took place under the sulfathiazole. In a case of acute osteomyelitis of the lower end of the humerus, pyrexia persisted after the administration of sulfathiazole but subsided on drainage of a subperiosteal abscess. The third case, acute osteomyelitis of the upper end of the femur, cleared up under sulfathiazole. The fourth case, affecting the lower end of the femur, showed pyrexia after drainage, which subsided under sulfathiazole. In the fifth case there was acute osteomyelitis of the ilium and suppurative arthritis of the hip. Blood culture yielded Staphylococcus aureus. No improvement followed sulfathiazole, the blood culture remaining positive. Of the five cases of carbuncle, recovery under sulfathiazole occurred in four and the fifth was still under treatment. Melton's experience was that large doses of sulfathiazole were necessary to achieve results comparable with those of sulfapyridine, but he was not prepared to make any comparison between the two drugs.

Indications for Removal of Tonsils and Adenoids

A reaction has taken place against operations for removal of tonsils and adenoids, which reached their peak about 1930. Thus in the Hospital for Sick Children, London, 4,730 operations were performed in that year, while in 1938 the number had fallen to 2,729. In opening a discussion at the Royal Society of Medicine on the Indications for Removal of Tonsils and Adenoids, Sir Lancelot Barrington-Ward said that the tonsil was in his experience much the more dangerous element. Its structure allowed organisms to lie dormant, to remain moderately but continuously active, leading to chronic general poisoning or flare-up into acute inflammation at indefinite intervals. Adenoids, on the other hand, acted only mechanically by obstructing respiration or by a low grade infection causing inflammation of the ear or cervical glands. The importance of adenoids was greatest in the earlier years of life and they might require removal within the first few months. If present in later years, the tonsils were usually also infected and it was wise to deal with both.

What were the conditions of the tonsils which demanded operation? The most usual description given was that they were large and septic, but the combination was not constant. Large tonsils might not be septic and septic tonsils might not be large. Mere size was not an indication for removal of a tonsil unless by reason of size it was injuring the patient. Sometimes a persistent cough might justify operation. More commonly there was obstruction to the food and air passages. A septic tonsil was a menace and should always be removed. How was it to be decided that a tonsil was septic? A standard appearance that would satisfy every observer was impossible and bacteriologic examination was not always helpful. More could be learned from the secondary effects, which might be direct or indirect. Among direct effects were: 1. Repeated attacks of tonsillitis, the only certain way of stopping which was removal. 2. Chronic enlargement of the upper deep cervical lymphatic gland, without enlargement of other glands, which always indicated tonsillar infection; such a gland was likely to harbor the tubercle bacillus of bovine strain; in the treatment of tuberculous glands, removal of the tonsils was essential. 3. Otitis media, with its sequels mastoiditis and deafness, which in the majority of cases were the result of infected tonsils and adenoids. Here a great advance of recent years was continuous medical supervision of school children and early treatment of the source of infection.

Indirect effects were less certain grounds on which the tonsil could be held responsible. In some it could be blamed only as a port of entry of a specific organism. To remove the

tonsil after the damage had been done was like shutting the stable door after the horse had been stolen. Tonsillectomy was reasonable only if there appeared to be continued infection or reinfection. Rheumatism with associated heart disease and chorea was a good example. The responsibility of selection here lay mainly with the physician. Chronic sepsis might have a wider effect. In a flabby child with scoliosis, knock-knee or valgus, chronic infection of the tonsils was not uncommon and the first part of the orthopedic treatment must be elimination of the toxemia. The least definite indication and perhaps the one that has brought most disappointment to the operator was recurrent or persistent nasopharyngeal catarrh and the common cold. If every cold began with a sore throat, removal of the tonsils might prevent further attacks. This was successful in the majority of cases, and if the colds returned they were less severe; but the wise surgeon would give no guaranty of immunity.

BUENOS AIRES

(From Our Regular Correspondent)

July 1, 1940.

Broadcasting of Health Programs

The national department of public health has recently organized popular radio lectures on the problems with which its various divisions deal. These lectures are delivered, generally by the heads of these divisions, over the government broadcasting stations. The first program for the month of June lists as topics milk and nutrition, maternal care and the work of the division of maternal and child welfare service, illegal practice of medicine, prophylaxis against influenza, the national department of health and drug addiction, functions of the health department, cooperation of parents with the eugenic program of the state, occupational diseases and accidents, hypertrophy and tonsillar infections, the public and the medical profession, significance of medical examinations in early infancy, and pertussis.

Malaria Control

Malaria control in Argentina is directed by a division of the national department of public health, with its seat in Tucumán. Dr. Carlos Alberto Alvarado, its director, was formerly general secretary of the national health department. Malaria in Argentina is not a problem of swamps but is endemically established in areas at the foot of mountains and occasionally in mountainous territory. The province of Buenos Aires with its long low littoral is free from malaria. Different species of Anopheles are found in the low coastal lands but they do not attack man. Anopheles pseudopunctipennis is the chief disseminator of malaria. The first efforts of the malaria control division were the draining of stagnant waters until it was discovered that swamps bred only mosquitoes harmless to man. While other species of Anopheles prefer to breed in quiet shady waters with luxuriant vegetation, Anopheles pseudopunctipennis seeks the banks of rivers and brooks exposed to light and air that produce weeds (algae spirogyrae) which are indispensable food to the malaria breeding variety. Paradoxically, drainage canals create dangerous breeding places. Waters with banks devoid of vegetation are found to breed the weeds favored by the malarial anopheles. These aquatic plants are easily crowded out by taller plants of more luxuriant growth but thrive where they have no overpowering competition. Along the course of drainage canals the algae spirogyrae thrive until stronger plants displace them. Canals built up with stone or cement were observed to prevent the ranker vegetation and thus furnished good harbor to the algae that bred the disease carriers. For this reason, needless clearing of drainage canals is also inadvisable as it attacks the more luxuriant plant growth. Cress such as Cardamina flaccida and burdock (Senecio cremeiplorum) set out to combat algae spirogyrae suffer from the disadvantage that rising water may kill them off.

Whether artificially watered rice plantations promote anopheles development has so far received no satisfactory answer. International observations seem to be contradictory. Alvarado conducted investigations in Tucumán and other northern provinces in which rice is grown. He found that irrigated rice fields were strongly favorable to the anopheles in question. On spleen examination the hematologic index of people living near the rice fields was higher than that of those living farther away. In regions infested with malaria a systematic "policing" of centers of infestation has been organized. Maps indicate the spots that are to be attacked. The species of Anopheles found in these regions is identified. Twice a year a general test is made, by means of the hematologic index, of infants 2 years old and younger native to the region. The index for the "epidemic type" is taken during April and May. This indicates the maximum level of malaria infection, that is, new and old infections. The index of the "endemic type" is taken in October and November. It indicates only the chronic infections. The age level of 0 to 2 was selected to make sure that the disease was not contracted elsewhere and because the presence of malaria parasites is best determined at this age. Tests made in one community in Tucumán based on 200 specimens resulted in 14.5 per cent positive reactions in October 1936. Subsequent tests gave a 5 per cent reaction in April 1937 and 1.5 per cent in October 1937. In one year malaria had been reduced by 90 per cent. The total malaria-infested area of Argentina is estimated at 120,000 square kilometers with 850,000 inhabitants. At present only 1,200 square kilometers has been given attention.

The annual report of the malaria control division of the national public health department for 1939 indicates that malaria incidence was within normal limits and showed a tendency to decline. Tertian malaria preponderated. More than 120,000 persons were treated. According to Alvarado's observations the frequency of congenital malaria is enormous. Several full-time positions have been created and three (of six) regional directors appointed.

Personals

Dr. Francis Scott Smyth of the pediatric department of the University of California has arrived in Buenos Aires for six months of research activity with Prof. B. A. Houssay.

Dr. Hernán Aguilar, associate professor at the faculty of medicine of Buenos Aires, has sailed for the United States to do research work at Washington University, St. Louis, on thoracic surgery.

Marriages

FRANK TURNER NORRIS, A. A. Surg. Lieut. (j. g.) U. S. Navy, Portsmouth, Va., to Miss Courtney Louise Taylor of Norfolk, May 24.

GALEN GLICK CRAUN, Huntington, W. Va., to Miss Beulah Genevieve Spencer of Richmond, Va., June 21.

GEORGE MILTON ROBINS, Louisville, Ky., to Miss Mary Frazier Kimbrough of Lexington, June 22.

CECIL CURTIS COLLINS JR., Jacksonville, Fla., to Miss Marjorie Winston of Durham, N. C., June 4.

EUSTACE VITOL CHAUVIN JR., Lafayette, La., to Miss Vanola Bailey of Austin, Texas, in June.

EMMETT STEVENSON LUPTON, Raleigh, N. C., to Miss Mary Paschal of Wake Forest, June 4.

EDWARD H. SIBLEY, Sioux City, Iowa, to Miss Clara Marie Munger of Grinnell, June 22.

FORREST ELLIOTT OGLESBY to Miss Mildred Virginia Garret, both of Norfolk, Va., June 8.

JOHN L. KLEIN JR., Muscatine, Iowa, to Miss Beatrice Kaiser of St. Paul, June 17.

JOHN A. LINEBERRY to Miss Jane Elizabeth Lassiter of Four Oaks, N. C., June 4.

Deaths

Joseph Williams Schereschewsky ⊕ Medical Director, United States Public Health Service, Boston; Dartmouth Medical School, Hanover, N. H., 1899; veteran of the Spanish-American War; in 1899 was appointed assistant surgeon in the United States Public Health Service and was promoted through the grades to that of medical director in 1930; from 1913 to 1918 was in charge of field investigations of occupational diseases; from 1918 to 1922 was assistant surgeon general in charge of the division of scientific research; was in charge of cancer investigations from 1922 to 1937; established a cancer research center at the Harvard Medical School in Boston; in 1935 was awarded the Distinguished Service Key of the American Congress of Physical Therapy; in 1937 organized the cancer control program for the state of Georgia; past president of the American Association of Industrial Physicians and Surgeons; member of the House of Delegates of the American Medical Association from 1918 to 1922; aged 67; died, July 9, at his summer home in West Harwich, Mass., of angina pectoris.

John Alexander Lanford ⊕ New Orleans; Medical College of Alabama, Mobile, 1905; instructor of anatomy at his alma mater from 1908 to 1910; instructor of surgical pathology from 1911 to 1914 and assistant professor of pathology and bacteriology at the Tulane University of Louisiana School of Medicine since 1914; past president of the Orleans Parish Medical Society; member of the American Association of Pathologists and Bacteriologists and the American Society of Clinical Pathologists; member of the board of directors of the American Society for the Control of Cancer; fellow of the American College of Physicians; served during the World War; aged 59; pathologist to the New Orleans Hospital and Dispensary for Women and Children; consulting pathologist to the United States Marine Hospital; director of laboratories and pathologist to the Touro Infirmary, where he died, July 2, of coronary thrombosis.

Edwin Pakenham Ruggles ⊕ Boston; Boston University School of Medicine, 1900; at various times lecturer, instructor, assistant professor, associate professor, professor and professor emeritus of obstetrics at his alma mater; member of the New England Obstetrical and Gynecological Society; fellow of the American College of Surgeons; consulting obstetrician to the Massachusetts Memorial Hospitals; served during the World War; aged 67; died, June 19, of cirrhosis of the liver.

Laurence Burton Sisson ⊕ Auburn, N. Y.; Syracuse University College of Medicine, 1912; served during the World War; on the staffs of the Auburn City Hospital and the Mercy Hospital; past president of the Cayuga County Medical Society; formerly physician in charge of the Auburn State Prison Hospital; aged 50; died, June 17; at the Strong Memorial Hospital, Rochester, of carcinoma of the bladder.

Martin Thomas Powers ⊕ Utica, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1905; member of the American Roentgen Ray Society and the Radiological Society of North America, Inc.; past president of the Utica Academy of Medicine; chairman of the New York State Roentgenology Society; aged 60; on the staffs of the Utica General Hospital and St. Elizabeth Hospital, where he died, June 14, of coronary thrombosis.

William Arthur Harvie, Regina, Sask., Canada; University of Toronto Faculty of Medicine, 1908; fellow of the American College of Surgeons; past president of the Saskatchewan Medical Association; on the staffs of the Regina General and Regina Grey Nuns' Hospital; surgical consultant, department of pensions and national health; served during the World War; aged 54; died, May 31.

Claude Burgess Williams, Elizabeth City, N. C.; University College of Medicine, Richmond, Va., 1903; member and formerly vice president of the Medical Society of the State of North Carolina; county health officer; at one time a trustee of the Agricultural and Mechanical College, Raleigh; formerly member of the local school board; aged 62; died, June 21, of cerebral hemorrhage.

B. Vernon Dickson, Covington, Tenn.; Memphis (Tenn.) Hospital Medical College, 1901; member of the Tennessee State Medical Association; past president and secretary of the Tipton County Medical Society; aged 63; died, June 30, in the Baptist Hospital, Memphis, of pleurisy with effusion, cardiac insufficiency and chronic tuberculosis of the lungs.

William James Vivian, Northport, N. Y.; Dartmouth Medical School, Hanover, N. H., 1912; member of the Massachusetts Medical Society, American Psychiatric Association and the New England Society of Psychiatry; on the staff of the Veterans Administration Facility; aged 55; died, June 10, of coronary thrombosis.

Edward Allen Pease ⊕ Pasadena, Calif.; Harvard Medical School, Boston, 1892; member of the Massachusetts Medical Society; formerly surgeon to the Boston Dispensary, Free Hospital for Women, Brookline, and the Carney Hospital, Boston; aged 75; died, June 19, of bronchopneumonia.

William A. Beach, Mankato, Minn.; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1893; member of the state board of medical examiners in 1906; formerly mayor of Mankato; aged 71; died, June 12, of cerebral hemorrhage.

Marie Olivier Becnel, New Roads, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1896; member of the Louisiana State Medical Society; for many years parish coroner; aged 66; died, June 26, of cerebral hemorrhage and arteriosclerosis.

Charles Edward Long, Williamsville, N. Y.; University of Buffalo School of Medicine, 1891; served during the World War; for many years county medical examiner; aged 70; died, July 4, in the General Hospital, Buffalo, of acute gangrenous appendicitis.

Murvington Emery Malaun, Carbondale, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1896; member of the Medical Society of the State of Pennsylvania; aged 72; died, June 25, of injuries received in an automobile accident.

Thomas J. O'Malley, Chicago; College of Physicians and Surgeons of Chicago, 1896; member of the Illinois State Medical Society; served during the World War; formerly member of the board of education; died, June 19, of myocarditis.

William J. Harlan ⊕ Bartlett, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1898; for many years president of the school board; aged 65; died, May 2, in a hospital at Temple of coronary thrombosis.

J. Sidney Hoffa, Williamsport, Pa.; Medico-Chirurgical College of Philadelphia, 1903; member of the Medical Society of the State of Pennsylvania; aged 60; died, June 12, in the Williamsport Hospital of pontile hemorrhage.

Russel Clark Paris, Hudson Falls, N. Y.; Regents of the University of the State of New York, 1883; member of the Medical Society of the State of New York; aged 80; died, June 16, of uremia and cerebral hemorrhage.

Roger Talmage Fox, Gloucester City, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1915; served during the World War; aged 51; died, June 22, in Florence of myocarditis and cirrhosis of the liver.

Joseph Goodman Knapp, Wyandotte, Mich.; Detroit College of Medicine and Surgery, 1915; served during the World War; on the staff of the Wyandotte General Hospital; aged 46; died, June 15, of encephalomyelitis.

Lorenzo Burton Zimmerman, Mount Carmel, Pa.; Jefferson Medical College of Philadelphia, 1894; member of the Medical Society of the State of Pennsylvania; aged 69; died, June 20, of coronary thrombosis.

Nelson A. Ludington, New Haven, Conn.; Yale University School of Medicine, New Haven, 1901; member of the Connecticut State Medical Society; aged 61; died, June 26, of hypertension and coronary occlusion.

George Hayward Coburn ⊕ Rangeley, Maine; University of Pennsylvania Department of Medicine, Philadelphia, 1875; aged 85; died, June 18, of bronchopneumonia, arteriosclerosis and cerebral hemorrhage.

Fitz Henry Farrington, Boulder, Colo.; State University of Iowa College of Medicine, Iowa City, 1893; member of the Colorado State Medical Society; aged 77; died, May 17, of cerebral hemorrhage.

Allen Andrew Van Slyke, Mount Jewett, Pa.; University of Buffalo School of Medicine, 1882; member of the Medical Society of the State of Pennsylvania; aged 81; died, May 30, of angina pectoris.

Ralph Semmes Jackson ⊕ San Antonio, Texas; University of Texas School of Medicine, Galveston, 1900; aged 70; died, June 25, in the Nix Hospital of fracture of the left femur and lateral sclerosis.

Frederick Warren McCaw ⊕ Colon, Neb.; John A. Creighton Medical College, Omaha, 1907; past president of the Saunders County Medical Society; aged 58; died, May 15, of heart disease.

Charles James Marquette, Nova, Ohio; Western Reserve University Medical Department, Cleveland, 1897; member of the county board of health; aged 69; died, June 20, of cerebral hemorrhage.

John Luke Hayden ⊕ Louisville, Ky.; University of Louisville Medical Department, 1909; served during the World War; aged 51; died, June 25, in the Norton Infirmary of pulmonary tuberculosis.

Josiah Murch Stanley ⊕ Northboro, Mass.; University of the City of New York Medical Department, 1884; school physician for many years; aged 80; died, June 4, of coronary thrombosis.

Fritzroy Farnsworth Pillsbury, Lowell, Mass.; Dartmouth Medical School, Hanover, N. H., 1909; member of the Massachusetts Medical Society; aged 55; died, June 18, in Saco, Maine.

Louis Valerio ⊕ Cincinnati; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1911; served during the World War; aged 54; died, June 4, of coronary thrombosis.

Edward Colfax McCurdy, Shellman, Ga.; Atlanta College of Physicians and Surgeons, 1902; member of the Medical Association of Georgia; aged 70; died, June 2, of arteriosclerosis.

Charles Henry Beadles, Racine, Wis.; John A. Creighton Medical College, Omaha, 1915; served during the World War; aged 53; died, June 8, in St. Catherine's Hospital, Kenosha.

John Porter Ferguson, Springfield, Mo.; Barnes Medical College, St. Louis, 1895; member of the Missouri State Medical Association; aged 69; died, May 6, of cerebral hemorrhage.

George Washington Smallwood, Pepperell, Mass.; University of the City of New York Medical Department, 1887; aged 78; died, June 21, of uremia and prostatic obstruction.

John A. Houser, West Salem, Ill.; Eclectic Medical Institute, Cincinnati, 1882; also a pharmacist; aged 81; died, June 28, in Quincy of uremia and hypertrophy of the prostate.

Cornelius Howard Duvall, Fort Worth, Texas; Louisville (Ky.) Medical College, 1901; served during the World War; aged 70; died, June 29, of acute pulmonary tuberculosis.

Clarence Hamilton Morris, Windsor, N. S., Canada; McGill University Faculty of Medicine, Montreal, Que., 1897; served during the World War; aged 67; died, May 22.

Jesse Thaxton Hayes, Oliver Springs, Tenn.; University of Nashville Medical Department, 1901; aged 66; died, June 28, in a hospital at Knoxville of injuries received in a fall.

William Cocke Lyons, Surgoinsville, Tenn.; Louisville (Ky.) Medical College, 1888; formerly bank president and member of the state legislature; aged 72; died, June 2.

John Clark Brown ⊕ Wichita, Kan.; National University Medical Department, Washington, D. C., 1900; aged 81; died, June 25, of myocarditis, cholecystitis and liver abscess.

Welles James Lowry, Carbondale, Pa.; Jefferson Medical College of Philadelphia, 1882; member of the Medical Society of the State of Pennsylvania; aged 84; died, June 9.

Alexander Campbell, St. John's, Newfoundland; McGill University Faculty of Medicine, Montreal, Que., 1902; F.R.C.S., Edinburgh, Scotland, 1910; aged 64; died, May 16.

Samuel Jacob Fryer, Muskogee, Okla.; Hospital College of Medicine, Louisville, Ky., 1902; member of the Oklahoma State Medical Association; aged 63; died, June 19.

John Abner Hawkins, Danville, Va.; Medical College of Virginia, Richmond, 1918; member of the Medical Society of Virginia; aged 44; died, June 7, of pneumonia.

William Kepler Parker, Dix, Ill.; College of Physicians and Surgeons, Keokuk, Iowa, 1883; member of the Illinois State Medical Society; aged 89; died, June 7.

Robert C. Sheetz ⊕ Orrick, Mo.; St. Louis College of Physicians and Surgeons, 1890; served during the World War; aged 73; died, May 25, of coronary occlusion.

Charles U. Patterson, Houston, Texas; Kentucky School of Medicine, Louisville, 1892; member of the State Medical Association of Texas; aged 76; died, June 6.

Caspar Wistar Miller, Wallingford, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1894; aged 71; died, June 24, of cardiorenal disease.

William Varner Wilcox, Sacramento, Calif.; California Medical College, San Francisco, 1899; aged 61; died, June 5, of chronic nephritis and heart disease.

Joseph Frank Mayes ⊕ St. Louis; Washington University School of Medicine, St. Louis, 1904; aged 62; was found dead in bed, June 27, of heart disease.

Ernest Druecilla Burden, Brookline, Mass. (licensed in Massachusetts in 1895); aged 65; died, June 9, of cerebral hemorrhage and arteriosclerosis.

Stephane Dulude, Dassel, Minn.; School of Medicine and Surgery of Montreal, Que., Canada, 1898; aged 66; died, May 12, of coronary thrombosis.

Cecile Lenore Greil, Los Angeles; Eclectic Medical College of the City of New York, 1910; aged 67; died, June 11, of hypostatic pneumonia.

G. Cloud Eshelman, Portland, Ore.; Hahnemann Medical College and Hospital, Chicago, 1890; aged 81; died, June 26, of cerebral hemorrhage.

Elmer Ellsworth Stone, Los Angeles; Cooper Medical College, San Francisco, 1890; aged 70; died, June 9, of carcinoma of the prostate.

Israel Baikovich, Chicago; Chicago Medical School, 1915; aged 65; died, July 8, in the Mother Cabrini Hospital of carcinoma of the prostate.

Ernest Henry Mercer, San Francisco; California Medical College, San Francisco, 1896; aged 72; died June 6, of carcinoma of the prostate.

Chester Walton Young, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1913; aged 52; died, June 16, of carcinoma.

Alma Sophia Larson Goude, Minneapolis; College of Medical Evangelists, Los Angeles, 1918; aged 52; died, May 1, of carcinomatosis.

Gilbert La Fayette Foster, Wolfville, N. S., Canada; University of the City of New York Medical Department, 1896; died, May 17.

Francisco Liano Parra, El Paso, Texas; Universidad de Guadalajara Facultad de Medicina, Mexico, 1923; aged 43; died in June.

Edgar J. Klotz, Allentown, Pa.; Jefferson Medical College of Philadelphia, 1886; aged 76; died, June 8, of acute coronary thrombosis.

John Hund, Peoria, Ill.; College of Physicians and Surgeons of Chicago, 1887; aged 86; died, June 23, in St. Francis Hospital.

Harry Leo Devine, Springfield, Mass.; Baltimore Medical College, 1909; aged 56; died, June 29, in the Wesson Memorial Hospital.

Benjamin Robert White, Strasburg, Va.; University of Maryland School of Medicine, Baltimore, 1896; aged 69; died, June 21.

Herbert Clarence Bolstad, Pescadero, Calif.; University of Illinois College of Medicine, Chicago, 1913; aged 56; died, June 29.

Leopold Freiberger ⊕ New York; University and Bellevue Hospital Medical College, New York, 1899; aged 72; died, June 2.

A. Le Grand Runion, Canonsburg, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1888; aged 89; died, June 11.

George Washington Hoglan, Bedford, Va.; Cincinnati College of Medicine and Surgery, 1885; aged 79; died, June 5.

Joseph L. Bennett, Kearney, Neb.; Eclectic Medical Institute, Cincinnati, 1874; aged 90; died, June 16, of acute nephritis.

George Ernest Cramer ⊕ Sharpsburg, Pa.; University of Pittsburgh School of Medicine, 1913; aged 56; died, June 14.

Andrew J. Learned, Millfield, Ohio; Columbus Medical College, 1877; Civil War veteran; aged 97; died, June 22.

Robert Rolen Preston, Glade Spring, Va.; Medical College of Virginia, Richmond, 1904; aged 61; died, May 2.

William Henry Deardorff, Philadelphia; Jefferson Medical College of Philadelphia, 1896; aged 72; died, June 20.

William F. Golling, Springfield, Ohio; Homeopathic Hospital College, Cleveland, 1887; aged 79; died, June 29.

Joseph William Field, Owensboro, Ky.; Kentucky School of Medicine, Louisville, 1901; aged 60; died, June 16.

Charles F. Sullivan, Ardmore, Okla.; Medical College of Alabama, Mobile, 1890; aged 76; died, June 6.

Napoleon T. Langlois, Wyandotte, Mich.; Detroit College of Medicine, 1891; aged 71; died, June 15.

Harold Canter, Philadelphia; Jefferson Medical College of Philadelphia, 1938; aged 26; died, June 9.

Thomas R. Evans, Seattle; Louisville (Ky.) Medical College, 1906; aged 65; died, June 19.

Correspondence

ABOLITION OF THE RETENTION CATHETER

To the Editor:—In the June 15 issue of THE JOURNAL appears an article by Dr. Richard P. Middleton entitled "A Plea for the Abolition of the Retention Catheter in the Preparation of Patients for Prostatic Surgery." While there can be little disagreement with most of the author's statements and he is to be congratulated on a satisfactory solution to a vexing problem, it seems hardly fair to consign this potentially valuable procedure to desuetude without first raising a voice in its defense. The picture that he draws—"the more or less tender urethra with crusted mucopurulent exudate clinging to the tape which fastens the catheter to the penis, and not infrequent copious oozing of pus around the catheter"—is unfortunately all too common, and it must be admitted that some method of improving such a situation is desirable.

That improvement demands complete discarding of the retention catheter in favor of intermittent catheterization does not necessarily follow. Attention to a few simple principles will eliminate the undesirable by-effects of the procedure which has obvious and well recognized advantages. Particularly is it advisable to call attention to these principles in view of the facts that even the author admits the necessity of the postoperative use of the retention catheter, that occasional cases requiring catheterization with the help of a rigid stylet do exist and that the services of a well trained orderly are not universally available.

The first of these principles is reasonable attention to surgical cleanliness. The patient should be prepared as for a surgical operation, the preparation including shaving the suprapubic, scrotal and perineal regions and thorough washing of the entire area with soap and water. Drainage tubes and the receptacle should be sterilized, the latter when full, being replaced by another previously sterilized rather than taken out, emptied and returned. If irrigations are necessary, and these should be carried out preoperatively only in badly infected cases, a closed irrigation system consisting of sterile reservoir, glass Y tube and drainage tube will eliminate the introduction of organisms which is almost inevitable if the hand syringe is used and the drainage tube disconnected for purposes of irrigation.

The second consideration has to do with the size of the catheter. The fallacy that a large catheter is necessary for adequate drainage has been responsible for many cases of urethritis, prostatitis and periurethral abscess. When it is considered that a No. 5 ureteral catheter working somewhat less than half time in accord with the peristaltic action of the kidney pelvis can provide ample drainage for the urinary output of one kidney, it seems obvious that the lumen of a soft rubber catheter as small as a No. 12 French will furnish satisfactory drainage of the bladder even with the large fluid intake desirable for prostatic patients. Fully as important as drainage of the bladder is provision for the exit of mucous secretions of the urethra. A large catheter occupying the full lumen of the meatus, which is the narrowest portion of the urethra, causes retention of these secretions, favoring bacterial growth and often resulting in purulent urethritis.

The third point is the elimination of adhesive strapping by the use of a Foley type catheter. A few years ago at my request C. R. Bard Company started the manufacture of a No. 16 catheter of this type. This size represented a compromise between my desire for one of smaller circumference and the technical difficulties of production. Experience has proved that it is small enough to allow proper drainage of the urethra in most cases. In cases in which there is reasonably good kidney function small doses of sulfanilamide, 15-20 grains a day (1 to 1.3 Gm.), provide added protection against infection.

The application of the foregoing measures have largely eliminated infection and urethral irritation, which appear to be the principal objections raised by Dr. Middleton to constant drainage. I agree entirely with him as to the advisability of operating in certain cases of prostatic obstruction without preliminary drainage, that infection should be avoided if possible and that "vaccination" of the urethra should be considered in the same category as "laudable pus." It has been my experience that all this can be accomplished by the proper use of the indwelling catheter.

Finally, I am not convinced that "being tethered to a bottle" is entirely a disadvantage. One of my patients was told by his son that what he needed to improve his health was a hobby, to which the old gentleman replied "Son, I have a hobby—keeping my water going." Possibly the responsibility of attending to his drainage apparatus may constitute one of the diversions which are as necessary to the well-being of the elderly patient as is physical activity.

SAMUEL N. VOSE, M.D., Boston.

EFFECTS OF VACCINATION ON WASSERMANN TESTS

To the Editor:—In the *Illinois Medical Journal* for January 1940, Dr. R. D. Barnard reports the case of a blood donor who after many successively negative serologic examinations suddenly became Wassermann positive. It was suggested that the change in reaction was due to the presence of vaccinia. Since vaccination and serologic testing is a routine procedure at this institution, it was an easy matter to make a statistical examination of this fact. One hundred patients (fifty male and fifty female) with known recent negative serologic reactions were vaccinated and the blood Kahn tests repeated at intervals varying between twenty-nine and seventy-six days from the onset of the vaccination take. In no instance was a positive Kahn reaction obtained. We conclude from this that if vaccinia produces a positive blood Kahn reaction it does so in less than 1 per cent of cases and that therefore patients with vaccinia and a positive serologic reaction still require intensive investigation to eliminate other possible causes of the positive result.

ALFRED PAUL BAY, M.D.
MANNING I. SANKSTONE, M.D.
Chicago State Hospital, Chicago.

ASPHYXIA OF THE NEWBORN

To the Editor:—Permit me to call your attention to an omission in the special article on Pediatric Emergencies by Dr. Joseph Brennemann, published in the March 16 issue of THE JOURNAL, page 956. Asphyxia of the newborn is discussed without mention of the possible occurrence of congenital atresia of the postnasal orifices as a cause. Such "complete bilateral occlusion can cause alarming asphyxia in the newborn. The instinct for nasal breathing in the newborn is so impelling that, unless the mouth is forced open or the choanal occlusion is immediately broken through, asphyxia may result. It is the opinion of many writers (Lebensohn, J. E.: Congenital Atresia of Postnasal Orifices, *Ann. Otol., Rhin. & Laryng.* **32**:1128 [Dec.] 1923. Cavanaugh, in discussion on Lebensohn. Clarke, J. P.: Complete Congenital Occlusion of the Posterior Nares, *Boston M. & S. J.* **138**:171 [Feb. 24] 1898. Richardson, C. W.: Congenital Osseous Obstruction of the Postnasal Orifices, *Ann. Otol., Rhin. & Laryng.* **22**:488 [June] 1913. Ronaldson, T. R.: Note on a Case of Congenital Closure of the Posterior Nares, *Edinburgh M. J.* **26**:1035, 1880-1881) that surely a number of deaths listed as 'asphyxia neonatorum' have been caused by unrecognized, complete, bilateral choanal occlusion" (Morgen-

stern, D. J.: Congenital Atresia of the Postnasal Orifices, *Arch. Otolaryng.* **31**:653 [April] 1940).

"In the newborn or in young infants, palpating with a probe or attempting to blow air through either nostril with a rubber bulb will help make the correct diagnosis. When the occlusion is membranous, rupture with a probe and dilation with the back of a small mastoid curet may give a satisfactory result" (Lemere, H. B.: Persistent Bucconasal Membrane in the Newborn, THE JOURNAL, July 31, 1937, p. 347).

It is important to emphasize to the obstetrician, pediatrician and general practitioner the fact that posterior congenital atresia exists and may be the cause of asphyxia in the newborn, requiring immediate relief.

DAVID J. MORGENSTERN, M.D., Brooklyn.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

TONSILLECTOMIES IN DIONNE QUINTUPLETS

To the Editor:—**Would you comment on the widely publicized wholesale tonsillectomies recently performed on the Dionne quintuplets? Those of us who try to protect the public from needless operations find it difficult to explain why such perfectly reared children should all at the same time have tonsils so diseased that they had to be removed.** **M.D., New York.**

[Because of the great interest of this inquiry it was referred to Dr. Allan R. Dafoe, who replied:]

ANSWER.—There appears to be an implied suggestion in the inquiry to the effect that the removal of the quintuplets' tonsils was an example of unjustified "wholesale" tonsillectomy.

First of all let me make clear that I am opposed to the removal of tonsils when it is not necessary. In the case of the Dionne quintuplets the children had been subject to recurring attacks of tonsillitis of growing severity over the course of between two and three years.

Probably the best method of justifying these operations is to quote from successive reports of Dr. Allan Brown, physician in chief, Hospital for Sick Children, Toronto, professor of diseases of children, University of Toronto Faculty of Medicine. Dr. Brown is one of the foremost pediatricians of Canada and in my position as medical guardian of the Dionne quintuplets I have from time to time had the benefit of Dr. Brown's consultations.

On Nov. 6, 1938, Dr. Brown examined the children and reported: "In general their health is excellent with the exception of their tonsils and adenoids, which are in a chronic state of inflammation, which already accounts for the enlargement of their cervical glands—this latter is palpable evidence that the infection from their tonsils is spreading and at any time may get into the whole system, producing disastrous results such as an involvement of the heart or joints or even severe generalized infection with death.

"It would be difficult for any one to assume further responsibility for these babies unless their tonsils and adenoids were removed at once. This procedure should be done on all five at once and should not be attended with risk under the able guidance of Dr. Dafoe."

After this report, it would have been criminal for me to delay further. The operations were performed on November 9. Dr. Brown was present and examined the tonsils and adenoids as they were removed. I quote from his report:

Marie: "Tonsils rub against one another in midline. They are fibrous, chronically inflamed and ulcerated in deep fissures. Each tonsil is firmly adherent to walls of fossa. . . . Large, flat, mushy adenoid tissue was removed . . . large postnasal space. . . ."

Annette: "Tonsils very large, pink, no deep fissures. Ulcerated in various areas. Areas of fibrosis and ulceration with hemorrhage were seen when the tonsils were removed. Each tonsil firmly adherent to walls of fossa. Large flat adenoid tissue, one third the size of the larger tonsil was removed. . . ."

Emelie: "Areas of fibrosis and chronic inflammation. About twenty points of chronic inflammation on these tonsils. Large and distended. Each tonsil firmly adherent to the walls of fossa. . . . Spherical, very large, ulcerated adenoid pad."

Cecile: "Tonsils nearly touch. Most of surface ulcerated. Soft, pulpy and some fibrosis. Some crypts filled. Each tonsil firmly adherent to walls of fossa. Large fibrous adenoid. . . ."

Yvonne: "Tonsils nearly touch in midline. Large. All the tonsil surface ulcerated. Tonsils one half the size of others but relatively large for her throat. Each tonsil firmly adherent to walls of fossa. Central form large mass of adenoid."

As a conclusion to this series of reports I quote from a report made when Dr. Brown visited the children on June 10, 1939, eight months after the operations: "It is a great source of satisfaction to see the remarkable improvement since the removal of their sources of infection. Their cervical glands (neck) are now normal and there is no sign of any deleterious effect that the diseased tonsils might have had. The operations will act as an insurance policy for their future health. . . ."

"As a result of this examination today I am able to say that it has amply justified Dr. Dafoe's decision to have their tonsils and adenoids removed last year. . . ."

I believe the foregoing series of reports constitutes an ample reply to the correspondent's suggestion.

As for the surprise expressed at the infection appearing in all five at the same time, I find that difficult to understand. I, on the contrary, would have been surprised if the infection had occurred only in part of the set. This is an identical set living in an identical environment. The appearance of a disorder in one individual and its failure to appear in others when no differences of heredity or environment exist would be surprising indeed to me.

As for the appearance of diseased tonsils in these children, I have no excuses to offer. It is well known that diseased tonsils occur in children of the best homes as well as those of the worst. We believe the care that has been given to these children is the best possible care we could have given them. These children are subject to outside sources of infection a great deal more than the public realizes, despite our attempts to protect them.

MYASTHENIA GRAVIS

To the Editor:—**A patient with myasthenia gravis of three years' standing has been taking prostigmine, ephedrine sulfate and glycolixir with but temporary improvement. His case has followed the typical course of this disease. His present condition is so distressing that I hope you can suggest some additional help.** **Jesse Shoup, M.D., Washington, D. C.**

ANSWER.—There is no "typical course" for myasthenia gravis. The disease progresses by remissions and relapses. The remissions may last for days, weeks, months or even years and the relapses for an equal length of time. Even when patients are at their worst, if they can be supported by large doses of prostigmine hydrobromide they may make an excellent recovery. Patients unable to chew, swallow, talk or lift their arms or legs or even their heads from the bed have recovered after weeks of illness. A few patients, moreover, have been carried through a difficult period of dyspnea by use of the Drinker respirator. If dysphagia is severe, prostigmine hydrobromide may be given by injection, and it is common with patients ordinarily taking prostigmine hydrobromide by mouth to use, on occasion, parenteral therapy. A nasal tube may be inserted when there is difficulty in swallowing, but this must be done with great care so that the tube does not, by mistake, pass into the larynx. Rectal feeding, or even intravenous medication with dextrose, is desirable. Every effort should be made to keep the patient normal both mentally and physically, for there is always a strong probability that, should he be carried through a severe attack, he will make a good and perhaps even a remarkable recovery. Prostigmine hydrobromide is by far the most dependable drug. It should be used in doses as high as from ten to fifteen 15 mg. tablets a day, or even more. Ephedrine sulfate is of some value in augmenting the effect of prostigmine hydrobromide. It should be given in doses of three-eighths grain (0.024 Gm.) three times a day.

The query does not give enough information on which to base any judgment with regard to the prognosis in this case. Although it states that the patient has been sick for three years, there is no indication as to whether the patient has had remissions and relapses, what muscles are involved, whether or not he has responded to prostigmine in large doses, and it does not state the doses that have been used. All these data would be necessary before a competent consultative opinion could be given. One would desire, moreover, to know the age of the patient. Viets and Schwab (The Diagnosis and Treatment of Myasthenia

Gravis, with Special Reference to the Use of Prostigmine, THE JOURNAL, Aug. 12, 1939, p. 559), in a study of forty-four patients observed by them over a number of years, lost four patients out of eighteen who were over 50 years of age but only one patient out of twenty-six under 50 years of age. Two of the patients in the older group who died failed to take prostigmine hydrobromide consistently. The most serious type of the disease, and the one that is usually fatal in spite of treatment, occurs in women from 18 to 25 years of age. In three cases of this type the response to prostigmine hydrobromide was never good, although large doses were used. The older patients, however, respond unusually well to this drug, and even when the patient is seriously ill the prognosis with regard to life is good.

MUSCULAR EXERTION

To the Editor:—**I have noted varying statements as to the effects of weight lifting on the human body. Would you please give me an opinion as to the possible harmful, as well as beneficial, effects which might result from (1) exercises using light weights a number of repetitions of which would be far below the limit of exertion or strain, i. e. exercises which result in general and increased muscular tonus, growth and strength, and (2) heavy, limit weight lifting which involves "supreme effort" types of exertion with previous training and with or without a warm-up. It would be of added interest to have your opinion on the effects after long periods of such lifting.** **Jack DeMent, Portland, Ore.**

ANSWER.—There is no unequivocal evidence as to either the immediate or the delayed effects of various forms of weight lifting. Perhaps the nearest approach to an answer is found in Dublin's report (*Harper's Monthly Magazine*, July 1928) that most college athletes have a greater life expectation than other men of their age group. The exceptions included some of the older athletes (who had had little or no medical supervision) and crew men. These last have a task that approximates "limit weight lifting." In this connection it is worth noting that farmers have a smaller life expectation than many other groups and that Prostestant ministers have a notably great longevity.

An important consideration is the age of the person in question. It is doubtful whether any form of weight lifting harms the well trained young man who is in good health, and even more doubtful that a "supreme effort" type of exertion is wise for most people after the third decade. As to the question of beneficial effects, it seems that the important considerations are, first, Do the exercises bring pleasure to the participant? and, second, Do the exercises impart grace and a sense of well-being? Solomon (Proverbs **20:***29*) has given good general advice:

> The glory of young men is their strength;
> And the beauty of old men is the gray head.

POSSIBLE MERCURY HAZARD FROM MERCURY CLUTCH

To the Editor:—**What is the possibility of mercury poisoning in an operator of a machine using a mercury clutch? This clutch is filled with mercury, which whirls around at great speed in the housing of the clutch. The housing is completely closed except for the opening of the tightly fitting shaft and two small openings which are closed by screw caps. The engineers who manufacture this clutch state that the loss of liquid mercury is negligible over a year's time and give as an estimate two or three drops in two years' time. There are from 3 to 6 ounces of mercury in each clutch. The heat generated is 270 F. During operation the operator has little or no need to handle this instrument. The question of poisoning was raised and although I thought that there was no danger I decided to ask your opinion.** **M.D., Ohio.**

ANSWER.—If, in fact, the total leakage of mercury is limited to "two or three drops in two years' time," no apprehension as to mercury poisoning need be entertained. Owing to the wearing of parts, it becomes an obvious possibility that in the course of time more leakage of mercury might arise than contemplated by the producing engineers. Metallic mercury sublimates at room temperature, which fact is of signficance. At a temperature of 270 F. sublimation naturally would be much more active. However, so far as known, a temperature of 270 F. within the clutch housing would not lead to the building up of a pressure of mercury vapors such as would tend to force any mercury out around the shaft in the absence of erosion. The nature of this machine is not disclosed in the query, but, if stationary, leakage would be observable. Any considerable leakage such as a daily drop should occasion concern. A selenium test paper is available which, in the presence of mercury vapors in the atmosphere, changes color. Such a test should be made from time to time. If evidence of seepage is thus provided, an exposure should be regarded as existing. From an engineering point of view it is possible to construct mechanical devices of this character without any leakage and therefore without prospective dangers of mercury poisoning.

SERUM OR PLASMA FOR TRANSFUSION

To the Editor:—**In view of the desirability of plasma transfusion as an emergency measure in the treatment of shock, is there any method of rapid coagulation or separation of plasma aside from centrifuging the specimen? What method would be the most rapid and satisfactory to obtain a clear plasma for transfusion when a centrifuge is not available and where banked blood or plasma is out of the question?** **M.D., Idaho.**

ANSWER.—Natural clotting of normal blood is relatively rapid (from two to ten minutes). Retraction of the clot is a slow process. Clotting of blood may be hastened by a variety of methods: whipping with glass rods, the addition of tissue extracts (thromboplastin, coagulins, thrombobinose) and the addition of foreign bodies such as glass beads. None of these methods are desirable, however, in the production of serum, and although coagulation is more rapid, the resultant clotted blood still requires centrifugation.

The collection of blood into an anticoagulant such as sodium citrate allows for the separation of plasma. Rapid separation of cells from plasma in unclotted blood also requires centrifugation. Otherwise several hours must elapse for natural settling of the cells.

Obviously, in the absence of a centrifuge, emergency plasma or serum preparation is not feasible. In view of the fact that serum or plasma may be stored for months if properly prepared in sterile containers, the logical solution to the problem would be to prepare serum or plasma in advance and to store it until needed, when it can be administered without any delay.

ACHING AND ITCHING HEELS

To the Editor:—**A man aged 45, Jewish, a salesman, has had itching and a dull ache in the heels of both feet for the past four years. These symptoms are continuously present but do not usually interfere with his sleep. At times, however, he has awakened from sleep because of itching in both heels. Immersing his feet in warm water has given relief. At different times various sorts of heel pads, arch supports and elastic stockings have been tried with only temporary improvement. The past medical history has been essentially negative except for an episode of lumbar pain about seven years ago, at which time the patient wore a specially made brace and slept on a board. The back does not cause him any pain at present. The tonsils were removed at that time because they were suspected of being a focus of infection. The family history is negative. The patient smokes about twenty cigarets daily. Physical examination was essentially negative. The weight was 150 pounds (68 Kg.), height 5 feet 9 inches (175 cm.). There was considerable dental repair. The blood pressure was 106 systolic, 74 diastolic. The heart, lungs and abdomen were normal. There were no significant orthopedic or neurologic observations. Peripheral vascular examination revealed the presence of dorsalis pedis and posttibial pulses in both feet. This was confirmed by a normal oscillometric reading in both ankles. There were no abnormal color changes in the elevated and dependent positions. The temperature of the feet was not abnormal. Histamine tests revealed a normal circulation in the skin at each ankle, calf and thigh. X-ray examination of the heels was negative. X-ray examination of the entire spine and pelvis showed hypertrophic arthritic changes in the third, fourth, fifth, sixth and seventh cervical vertebrae. The thoracic spine was normal. Complete blood, urinalysis and blood Wassermann tests revealed no abnormalities. A spinal puncture revealed normal dynamics and normal microscopic and protein content. The spinal Wassermann and colloidal gold tests were negative. A paravertebral procaine block was performed on the right side. Three cc. of 1 per cent procaine hydrochloride was injected alongside the bodies of the second, third and fourth lumbar vertebrae. This injection resulted in a prompt rise in the skin temperature and increase of oscillation, which gave evidence of complete sympathetic paralysis. In spite of this anesthesia the pain in the heel was not relieved. Vitamin B_1 was given in 20 mg. doses intravenously daily for two weeks without result. The patient then stopped smoking abruptly with complete alleviation of the foot symptoms but he then had a constricting sense of pressure in the throat, not relieved by sedation or antispasmodics. He ascribed the throat symptoms to the cessation of smoking and after about four weeks he resumed his smoking habit. The result was that the sense of pressure in the throat disappeared in a few days and the foot symptoms reappeared in a few days and gradually regained their former intensity. Several months later he again experienced relief of foot symptoms when he ceased smoking and as before the throat symptoms developed so that he again resumed smoking. The result was that the throat symptoms disappeared and the itching and pain of the heels reappeared. What additional procedures or studies do you advise? Are such pressure symptoms in the throat known to occur when a habitual smoker stops smoking abruptly and completely? Would it be advisable to narcotize the peripheral nerves of the legs?** **M.D., Pennsylvania.**

ANSWER.—It is improbable that the situation described indicates organic disease, for thorough investigation has failed to demonstrate evidence of organic disease and there are signs of nervous instability. No reason is known why cessation of smoking caused disappearance of the distress in the heels unless this distress was psychogenic in origin. The occurrence of the constricting sensation or pressure in the throat on cessation of smoking is almost certainly psychogenic. It is suggested that the situation presented be surveyed thoroughly from the standpoint of a functional disturbance rather than from the standpoint of an organic disease.

AMBULATORY AUTOMATISM OR FUGUE

To the Editor:—I am 62 years old, 6 feet (183 cm.) tall, weigh 212 pounds (96 Kg.) and never had any serious sickness. I had influenza twice, both attacks mild, and was in bed about two days each time. I have never tasted alcoholic liquors of any kind and have been moderate in all my habits. I have just had a general physical check-up; the head and chest were roentgenographed, the Wassermann test was made, the urine, reflexes and eyes were checked, all with negative results. The blood pressure was 140 systolic, 90 diastolic. The heart was normal except that the aorta looked a little large. My complaint is this: About twenty years ago I was going on a night call when suddenly I appeared to be going in the opposite direction. Through reasoning I found the patient's home, examined him and treated him and got almost back to town when I suddenly became normal again. Then only a few nights after that I was returning from a country call and had it happen again. This time it was more persistent. I could not right myself after getting to town so stopped at my office and saw several patients who were waiting, yet all the time my directions were reversed. My office seemed on the wrong side of the street and the rooms in my office seemed in reverse order. I was afraid to try to go home alone as all the houses seemed to be on the reverse side of the streets, but on going into my house I instantly righted myself. There is no dizziness, no headache or nausea and my mind is perfectly clear except in orientation. Since then every time I come in my office at night the moment I enter my directions have become reversed and they stay that way until I go home, when I am suddenly righted. I never have had any indication of the trouble in the daytime. I have been examined by several good men but none ever heard of just such a case. It appeared to all that my center for orientation has gone haywire, but why or what caused it or how to combat it or what the outcome will be no one seems to know. I should like your opinion on diagnosis, prognosis and treatment and references if there are any.

M.D., New York.

ANSWER.—From the evidence submitted it appears that this is what is known as an ambulatory automatism. This is also known as a fugue or a psychic equivalent. This condition is related to epilepsy and occurs usually in place of the convulsion. There may be a complete amnesia for the attack or there may be complete retention of all facts during the attack. The attacks may last for minutes, hours or days. Usually when the attack lasts longer than minutes or an hour or two one must think of a hysterical reaction. From the history there is a loss of orientation in the attack. It is suggested that a physician administer sodium bromide 1 Gm. three times daily and increase the dosage gradually if and when the attacks do not cease. Have there ever been convulsions or loss of consciousness as a child or as a young adult? If the correspondent is unable to take bromides he can use phenobarbital in doses of 0.1 Gm. two or three times daily. The following books may be consulted:

Oppenheimer, Hermann: Text-Book of Nervous Diseases for Physicians and Students, Edinburgh, Otto Schulze & Co..

Jelliffe, S. E., and White, W. A.: Diseases of the Nervous System, ed. 6, Philadelphia, Lea & Febiger, 1935.

Dercum, F. X.: A Clinical Manual of Mental Diseases, ed. 2, Philadelphia, W. B. Saunders Company, 1917.

There is apparently no objective evidence of organic disease of the central nervous system in this instance. Lesions in the occipital and temporal lobes may cause auras or sensations such as described.

DISINTEGRATION OF WOOL DIAPERS

To the Editor:—Several mothers do not use rubber pants over the diapers of their infants. Instead they prefer a knitted wool pantalet. In one particular case the wool rapidly disintegrates and the structure falls apart. The baby is taking minute doses of iodine and is also taking cod liver oil, purified vitamin D in propylene glycol and ferrated maltine. These same substances are being taken by other babies, whose mothers are not experiencing the same trouble. The diapers in this case have been treated with mercury bichloride without any effect on the degeneration of the wool. Can you inform me what agent is acting to cause this process to continue?

M.D., Minnesota.

ANSWER.—As in this particular case the wool of the diaper disintegrates and falls apart, whereas it does not do this with other infants using the same type of diaper and taking the same medications, there are only about two possible explanations. (It is presumed that the diaper is of the same manufacture as those being used by the other infants. If not it might be wise to obtain diapers of the same manufacture because there is considerable variation in the price of diapers and their quality even in the same style of diaper or pantalet.) Either some agent is used in the washing of the diaper different from those used for the others or there is some peculiar chemical in the child's urine causing the disintegration of the wool (a high content of ammonia might conceivably cause trouble). If this baby's diaper after the urine has remained in it for some time smells strongly of ammonia, then this should be controlled in one or all of the following ways: by rinsing the diaper last in saturated boric acid solution; cutting down the fats in the baby's diet, or adding one-fourth teaspoon of baking soda to each bottle of the formula for a week or so. Free ammonia is not present in the urine when first passed, and it is possible that soaking the diapers in water immediately after being wet might dilute the ammonium salts sufficiently before ammonia forms in considerable amounts.

BLEEDING FROM GUMS

To the Editor:—A white woman aged 53 complains of bleeding from the gums, especially in the morning before brushing her teeth. She has had this condition for the last fifteen years intermittently, and in spite of taking large amounts of fruit juices, ascorbic acid and calcium recently there has been no improvement. The gums are in perfect condition as confirmed by her dentist, and no lesions are apparent in the mouth. She does not bruise easily nor do any purpuric spots appear spontaneously. Her blood pressure is 170 systolic, 120 diastolic. The urine is completely normal. The red count is 4,310,000; hemoglobin content 72 per cent. The white count is 8,950, polymorphonuclear leukocytes 52 per cent and lymphocytes 48 per cent. The coagulation time is seven minutes. The platelet count is 408,000.

Alvin A. Rosenberg, M.D., Morristown, N. J.

ANSWER.—Without more detailed information the question can be answered only by assuming what might be the relationship between the physical conditions mentioned and the oral condition, since the statement is made that "the gums are in perfect condition." Presumably the bleeding is nothing more than capillary oozing which causes the saliva to be blood tinged. Since the bleeding has been intermittent, it is possible that the condition is associated with the menstrual periods, if still existent. This question should be carefully checked. The literature contains reports of sex hormones being associated with gingival disorders. Although it is impossible to make definite statements regarding the relationship of the complaint to the blood picture, some obscure hemorrhagic diathesis on which is superimposed a low grade chronic inflammation of a septal gingiva in a posterior segment of the dental arch can be considered. Lastly, one would suggest consideration of the entire group of vitamins, more especially A, B and K. It might be of value to determine the ascorbic acid level of the fasting blood plasma on the basis that the patient was not capable of utilizing all the ascorbic acid taken in the diet or administered as a supplement.

REFRACTORY PRURITUS VULVAE AND ANI

To the Editor:—A woman more than 70 years of age has been suffering from pruritus vulvae and ani for the last five years. The pruritus is combined with a senile vaginitis, kraurosis and leukoplakia of the tongue. In the night time especially the itching is bad and sedatives such as the bromides and barbiturates often aggravate the itching. In the last few months the itching developed on her feet and there was a burning sensation of the tongue. There is oftentimes an itching around the lips. All laboratory examinatons, including blood sugar, blood calcium, vaginal smear and stool, showed negative results. There was a moderately increased blood sedimentation rate. Local treatment consisting of high voltage x-rays, ultraviolet rays, alcoholic injections, estrogenic injections and estrogenic hormones in vaginal suppositories, polyglandular injections, thyroid tablets, vitamin B_1 hydrochloride, later vitamin B complex, nicotinic acid, alkalizing of the system, calcium, various tonics and vaginal instillation of 3 per cent tannic acid in glycerin, kaolin ointments, insulin injections and a purine-poor diet did not give any improvement. The patient is excitable, nervous and unable to sleep. She admits that the nervousness aggravates her condition and if she is occupied the itching subsides a little. The nicotinic acid injections, 50 mg. given every other day, altogether six injections, gave her an urticaria-like reaction. She does not want to continue because she did not see much progress. Kindly advise me what kind of treatment would come into consideration. What kind of sedatives, if any, in injection form would be advisable? Would continuance of the nicotinic acid (perhaps in highest doses of 100 mg.) be advisable? Kindly explain what the urticarial reaction is due to.

M.D., New York.

ANSWER.—The patient has had almost the entire gamut of therapeutic measures generally used to treat pruritus vulvae and ani and other forms of pruritus. Perhaps, however, none of these substances have been given a thorough enough trial. What the patient most likely needs is a combination of a sedative, local soothing applications and estrogen therapy. Any one of the mild sedatives which does not produce disagreeable symptoms should be prescribed for a number of days at a time. Perhaps small doses of chloral hydrate or barbiturates may be tolerated by the patient. There is no need to administer the sedatives by injection. Furthermore internal estrogenic therapy may be given for a brief period. Long continued administration of estrogenic substance should be discouraged, and careful inquiry should be made of the family history. Temporary relief may be obtained by using cold compresses locally. In some cases heat helps but in others it aggravates the itching. The application of pure honey has given relief to some women. A lotion or salve containing phenol or sodium thiosulfate may also be helpful temporarily while waiting for the estrogens to take effect.

The patient should be advised to avoid rubbing the involved parts when cleansing the anus and vulva after a bowel movement or urination. The parts should be patted and not rubbed and it is best to use soft cotton or soft tissue rather than ordinary toilet paper. Scratching aggravates the condition; hence the patient should be advised to pinch the part which itches or, better still, make firm continuous pressure on the part with the closed fist or a few fingers. Since the nicotinic acid gave the patient an urticaria-like reaction which added more areas of itching, this medication had better not be repeated.

Suggestive therapy in the form of informal psychotherapy may be helpful.

GROWTH OF LONG BONES

To the Editor:—**What would be the proper management of the following case? A 7 year old boy whose birth date is November 1932 was injured in an automobile accident in June 1937. A compound fracture of the left tibia in the region of the ankle resulted. Osteomyelitis at the site of the fracture developed about four weeks after the accident. The leg brace was removed one year ago. X-ray examination shows complete loss of growth at the lower tibial epiphysis. The left tibia is three fourths of an inch shorter than the right. The left foot is slightly "turned in" at the ankle as a result of the continued growth of the left fibula at both its epiphyses and the stoppage of growth at the left epiphysis of the left tibia. The boy apparently walks at a normal gait and runs and jumps without any pain. The leg has not drained for about one and a half years. The external malleolus of the left foot is slightly more prominent than the right external malleolus. The boy's parents and his brothers and sisters average about 5 feet 4 inches (162.5 cm.) in height. How much of the tibial longitudinal growth takes place at the upper epiphysis and how much at the lower epiphysis? What is the rate of growth of the tibia and fibula at the various ages from the time of birth to the time of normal complete ossification of its epiphyses? Approximately how much more growth (average) of the lower legs at the lower epiphyses can be expected until growth ceases? At what age do the two epiphyses of the tibia become fused? Would a brace be advisable to prevent any further deformity? Would a shoe with the outer portion of the sole and heel slightly thicker than the inner portions be advisable in an attempt to prevent further deformity? Would a resection of the left fibula including removal of the lower cartilage plate be advisable now or later? Would osteotomy for lengthening the tibia be advisable now so far as the tibia has been the site of a previous osteomyelitis? Should stoppage of growth of the lower epiphyses of the two bones of the sound lower leg be instituted at the time of resection of the left fibula and operative intervention to prevent further growth at its lower (left fibula) epiphysis? Should the scar at the site of the injury be removed? When? How far would "inversion" of the foot progress if left untreated? What complications would arise if the foot should be left unmolested until bony growth in the long bones of the leg ceased? The left ankle joint (intra-articular surfaces) is normal in every respect.**

M.D., Michigan.

ANSWER.—Most of the growth in the lower extremity occurs in the region of the knee joint. Piersol gives the eighteenth and nineteenth years as the periods in which the lower epiphysis of the fibula unites and the eighteenth year for the ossification of the lower epiphysis of the tibia. Dr. Dallas Phemister, of the University of Chicago, has been a pioneer in this country in the arrest of the growth of the epiphysis to produce shortening in sound limbs. Reference to his writings will give much information. Each patient is an individual problem, and a definite answer such as this inquiry requires cannot be given.

SISAL FIBER, OR HEMP, AND ALLERGY

To the Editor:—**Have you any information as to the allergic properties of sisal fiber as used in mattresses? Are there any known cases on record of sensitiveness to this product? To what group or family of plants is it related?**

Francis J. Cenedella, M.D., Moline, Ill.

ANSWER.—A search of the literature has revealed no report as to the allergic properties of sisal fiber, or hemp (henequen), which is the product of the Agave rigida variety of sisalana. Agave is a member of the order Amaryllidaceae; the century plant, Agave americana, is the best known species of the genus. An inferior fiber is obtained from another species, Agave decipiens. The fiber is obtained from the leaves. In conjunction with manila or alone it is used extensively for cordage and binder twine. The plants grow extensively in Florida, the Bahamas, the West Indies, Yucatan and other parts of Central America.

According to a letter from Berlin (THE JOURNAL, Aug. 5, 1939, p. 522) Lehmensick read a paper before the Medizinische Gesellschaft of Bonn in which he stated that during the course of an expedition to Tanganyika in 1938 he found that pneumoconiosis, sometimes followed by tuberculosis, occurred in native workers. In the preparation of sisal the native brushes hemp on brushing machines, forming great clouds of dust which consist of small hemp fibrils and earth dust from the plants and which cover the workers like layers of flour. It has been estimated that the worker in such shops can endure the work for seven or eight years at most.

LACQUER SPRAYS IN BEAUTY PARLORS

To the Editor:—**I should like to know the active ingredients of the lacquer spray used in beauty parlors. Is there any reason to believe that a beauty operator using such a spray over a period of time would develop a peribronchial pulmonary fibrosis?**

M.D., Wyoming.

ANSWER.—A variety of commercial hair lacquers are available to beauty parlors, every one different as to constituents and quantities of constituents employed. A typical formula for a heavy hair lacquer is:

Resin	15 parts
Sandarac	10 parts
Benzoin (Siam)	20 parts
Alcohol (96%)	50 parts
Perfume	5 parts

The possibility exists that operators may become sensitized to the resinous constituents of lacquers and may present manifestations of cutaneous disease, asthma, bronchitis and the like. In fact, cutaneous diseases among beauty parlor operators are fairly common, but since so many chemicals may be used it is difficult to determine the offending agent. It is not possible to state that a peribronchial pulmonary fibrosis is a characteristic result of exposure of any duration or severity to hair lacquers.

SALTPETER IN FOOD

To the Editor:—**Recently I have received many inquires from students and parents regarding the use of saltpeter in food in institutions, allegedly for the purpose of reducing sex interest. Some persons are so convinced that this is being done that they attribute menstrual disturbances, which frequently follow a change of environment, to this drug. I can find nothing in pharmacopeias indicating that it has such a function, nor do I know that it or any other drug has been used in this way. Yet there are people who are positive that institutions employ it, and I should like to quell this rumor once and for all here.**

M.D., Texas.

ANSWER.—Saltpeter is said to be used extensively in institutions and camps, but there are no published statements that could be quoted, and rumors are often based on queer tasting coffee, which may have other causes. The anaphrodisiac action, if any, is probably largely suggestive, but it is imaginable that the general depressant action of continued use of the drug might have such a result. No critical observations have been reported, nor is the effect discussed in modern books; but Stillé in his "Therapeutics and Materia Medica" (Philadelphia, Lea & Febiger, 1874, p. 613) states, under Potassium Nitrate, "In the last century, Alston described it as resolvent, antiseptic, antiphlogistic, diuretic, purgative and anaphrodisiac." Contrary to popular rumor, saltpeter is not valuable as an anaphrodisiac, and its use by cooks or other laymen in institutions cannot be too strongly condemned.

SENSITIVITY TO SERUM

To the Editor:—**On a form for medical examination used by the Boy Scouts of America (catalogue 4/26, form C-950) the following question is asked: "Do you think this boy is likely to be sensitive to serum inoculations?" In the absence of a suggestive history the only way I could give the desired information would be by use of cutaneous tests with serum. Please tell me something along this line that will help to judge individual sensitivity to serum? I have had some odd reactions with injections of serum in persons who apparently present nothing to indicate untoward reactions; hence as a routine I always have epinephrine at hand.**

Frederick J. Simmonds, M.D., Boston.

ANSWER.—In the absence of a history of asthma or information concerning any allergic condition, it is not possible to judge that an individual is sensitive to serum unless appropriate tests are made. As the majority of serums are from the horse, it is likely that an individual sensitive to one specific serum would also be sensitive to most other serums.

FREQUENCY OF SCHICK TESTS AND REVACCINATION

To the Editor:—**In doing school work I encounter considerable disagreement among the profession as to how often Schick tests should be given children who have previously had a negative test. Will you kindly inform me what the best opinion is? Another question on which there is disagreement is how often children should be revaccinated.** **M.D., Indiana.**

ANSWER.—If the Schick test is negative in an individual who has not been immunized artificially against diphtheria by the customary means, it should not be necessary to repeat the test on future occasions. However, when a negative Schick test has been secured as the result of immunizing inoculations, future Schick tests should be performed for the purpose of determining the duration of the immunity that was artificially established. The length of time artificially induced immunity endures depends on the antigenic material and the dosage used. Under some circumstances it would be well to perform a Schick test once a year whereas, if the best procedures for active immunization

are followed, the average immunity should last from three to five years or even longer. Then Schick tests could be repeated after such intervals of time have elapsed.

If a child was successfully vaccinated during the first year of life and revaccinated successfully when entering school, immunity, in most instances, would probably endure for life. Some health departments recommend that revaccination be performed every five years. Regardless of any past vaccinal history, every individual should be vaccinated immediately after any known exposure to smallpox. An individual with a typical vaccination scar seldom contracts smallpox.

ORDER OF IMMUNIZATION IN CHILDREN

***To the Editor:*—What routine procedure of immunization is indicated in a child, according to the best present day practice? At what ages and in what order should they be applied? How often should they be repeated?**
M.D., Colorado

ANSWER.—It is well to perform vaccination against smallpox within the first three months after birth. Next in order, immunization against whooping cough is advocated by many. Ordinarily this procedure is not advised prior to the second half year of life. As a rule, when the child has reached 9 months of age it should be immunized against diphtheria. At this time the combined method of establishing immunity against both diphtheria and tetanus may be adopted. Between the ages of 1 and 2 years consideration may be given to inoculation of the child with streptococcus toxin for the purpose of establishing immunity against scarlet fever. Some hesitate to resort to the last named procedure because of the possibility of severe reactions. Vaccination against smallpox should be repeated when the child enters school and again before entering college. Schick and Dick tests should be done when school age is reached in order to determine whether further immunizing substances are required.

CONVALESCENT SERUMS FOR CONTAGIOUS DISEASES

***To the Editor:*—Please send me information on convalescent serum for measles, mumps, whooping cough and scarlet fever. Also please advise where they can be obtained.** **H. E. Mobley, M.D., Morrilton, Ark.**

ANSWER.—Human convalescent serum is of value for the prevention of measles and scarlet fever if given soon after exposure in doses of 5 to 10 cc., depending on the age of the patient. Meader of Detroit has reported good results with convalescent serum for the prevention of whooping cough. For mumps prophylaxis convalescent serum is adopted less frequently than for the other diseases mentioned. Human convalescent serum has been used for the treatment of each of these diseases but is undoubtedly of greatest value in scarlet fever.

In the Middle West there are the Milwaukee Serum Center and in Chicago the Samuel Deutsch Serum Center at Michael Reese Hospital. The Detroit Department of Health also maintains a center for the preparation of human convalescent serums.

Further information may be obtained from an article by A. L. Hoyne, "Immunologic Methods in Pediatrics" (THE JOURNAL, April 22, 1939, p. 1581), also from an article by Hoyne, Levinson and Thalhimer, "Convalescent Scarlet Fever Serum" (*ibid.*, Sept. 7, 1935, p. 783).

STAINED TEETH FROM FERROUS SULFATE

***To the Editor:*—What can be done to prevent staining of the teeth in anemic children when ferrous sulfate in powder form is administered?**
Harry Wexler, M.D., Brooklyn.

ANSWER.—The discoloration of teeth from the use of ferrous sulfate in the treatment of anemia is superficial and does not penetrate the tooth substance. A thorough prophylaxis which removes the film deposited on the surface of the teeth will remove this stain. There should be little discoloration if the ferrous sulfate is given in tablet or capsule form or if it is prescribed in a heavy syrup.

COMPLICATIONS AND PROGNOSIS IN BURNS

***To the Editor:*—1. Please give me some information regarding the prognosis of a first degree burn that covers more than half the body. 2. Is nephritis the most common complication of burns over a large surface of the body?** **J. O. McKenney, M.D., Beaver Dam, Ky.**

ANSWER.—1. The prognosis of a first degree burn that covers more than half the body is good. This has been proved many times by individuals suffering from extensive sunburn.

2. The most common complication of burns over a large surface of the body is infection and toxemia. Nephritis would be considered a part of the complication of toxemia.

Medical Examinations and Licensure

COMING EXAMINATIONS

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, August 3, page 406.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II, Sept. 11-13, to be given in medical centers having five or more candidates desiring to take the examination. Part III, Baltimore and New York during October and Boston during November. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various centers, Feb. 20. Final date for filing application is December 21. *Oral.* Cleveland, preceding A. M. A. convention. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Various centers, Oct. 28. Applications must be on file not later than Sept. 16. *Oral.* Chicago, Dec. 6-7. Applications for Group A must be on file not later than Nov. 1. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* October 21. Applications must be on file not later than September 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Chicago, Oct. 18-19. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Cleveland, Oct. 5. *Written.* Various centers, March 8. *The only written examination during 1941.* Applications must be on file not later than Dec. 1. A special oral and clinical examination will be held on the Pacific Coast during 1941 providing there will be enough candidates to warrant it. Applications for this examination should be on file not later than Sept. 15. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and written.* New Orleans, January 1941. Final date for filing application is November 15. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PEDIATRICS: New York, March 30-31. Following the Region I meeting of the American Academy of Pediatrics. Chicago, May 18. Following the Region III meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral.* New York, December 18-19. Final date for filing application is October 8. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Boston, Sept. 26-29. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Part I. Various centers, October 21. Final date for filing application is September 15. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Oral and Written.* Chicago, February 1941. Applications must be on file not later than Oct. 15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

New York Endorsement Report

Mr. Herbert J. Hamilton, chief, Bureau of Professional Examinations, reports fifty-one physicians licensed by endorsement from March 31 through June 29. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists		(1939)	N. B. M. Ex.
Colorado School of Medicine		(1902)	Colorado
University of Colorado School of Medicine		(1926)	Colorado
Georgetown University School of Medicine		(1938)	N. B. M. Ex.
Emory University School of Medicine		(1938)	N. Carolina
Northwestern University Medical School		(1939)	N. B. M. Ex.
Rush Medical College		(1937)	N. B. M. Ex.
The School of Medicine of the Division of the Biological Sciences		(1938)	N. B. M. Ex.
Indiana University School of Medicine		(1932)	Indiana
University of Kansas School of Medicine		(1932)	Puerto Rico
Johns Hopkins University School of Medicine		(1937)	Maryland
Boston University School of Medicine		(1936)	N. B. M. Ex.
Harvard Medical School		(1933),	(1938) N. B. M. Ex.
Tufts College Medical School		(1938)	N. B. M. Ex.
Wayne University College of Medicine		(1937)	N. B. M. Ex.
University of Minnesota Medical School		(1939)	Minnesota
St. Louis University School of Medicine		(1925)	Missouri
Washington University School of Medicine		(1938)	N. B. M. Ex.
Columbia University College of Physicians and Surgeons		(1933)	New Jersey, (1937), (1938) N. B. M. Ex.
Cornell Univ. Med. College (1935), (1936), (1937),		(1938)	N. B. M. Ex.
Long Island College of Medicine		(1938)	N. B. M. Ex.
New York Med. College and Flower Hospital (1936),		(1937)	N. B. M. Ex.
New York Medical College, Flower and Fifth Avenue Hospitals		(1938, 5)	N. B. M. Ex.
New York University College of Medicine		(1937, 2)	N. B. M. Ex.
University and Bellevue Hospital Medical College		(1935)	N. B. M. Ex.
Eclectic Medical College, Cincinnati		(1939, 2)	Ohio
Western Reserve University School of Medicine		(1935)	Ohio
University of Cincinnati College of Medicine		(1939)	N. B. M. Ex.
Jefferson Medical College of Philadelphia		(1938)	N. B. M. Ex.
Vanderbilt University School of Medicine		(1936)	N. B. M. Ex., (1937) Tennessee
University of Vermont College of Medicine		(1936)	N. B. M. Ex.
University of Virginia Department of Medicine		(1938)	Virginia

University of Wisconsin Medical School.....(1937) Wisconsin
McGill University Faculty of Medicine.....(1937)N. B. M. Ex.
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin .....(1936)N. B. M. Ex.
Regia Università degli Studi di Roma. Facoltà di Medicina e Chirurgia .....(1937) New Jersey
Université de Genève Faculté de Médecine.....(1935) New Jersey

Book Notices

As I Remember Him: The Biography of R. S. By Hans Zinsser. Cloth. Price, $2.75. Pp. 443. Boston: Little, Brown & Company, 1940.

Already widely celebrated by numerous reviews in literary publications, this volume by Dr. Hans Zinsser may be recommended as required reading for every young physician who wishes inspiration, and for every older physician who can appreciate the best in the field of medical literary contributions. It was selected by the Book of the Month Club as its choice for July.

Assuming a somewhat unusual technic, Dr. Zinsser discusses his own life as if it were that of a dear friend with whom he was intimate. The flavor of the book is that of soft reminiscence, modified by writing full of strength, modified by scientific historical records, modified by philosophic cogitation, all of which makes it extraordinary beyond any other personal memoirs that have become available. Comparison may be odious, but this autobiography stands high above any of the popular autobiographic contributions to medicine that have regaled the public during the past few years.

Here are first hand accounts of many of the scientific great and near great who have occupied the medical scene during the past four decades. Here are evaluations of psychoanalysis and the place of women in science and in life. Here is a defense of physicians' conservatism which deserves quotation:

> To a moderate degree, then, conservatism is useful. But by far the more important causes of lag lie in the nature of the work which medicine is called upon to perform. The doctor's profession is, in part, an art, since it deals with matters that demand manual skill; in part, again, it is a branch of that vague middle ground between the physical and the psychological, in which emotional intelligence and great sanity of judgment are required; it is, like all biology, an application to an unlimited variety of problems of the reasoning and the technics of all available science.

For every one recently interested in the discussions of socialized medical practice, this point of view deserves consideration:

> At the present time, there is a strong popular movement for the socialization of medical practice, and an effort, essentially praiseworthy, to bring the benefits of discovery and of improved care within the reach of the population as a whole, irrespective of ability to pay. This is as it should be, and there is little question of the fact that the old system of charity clinics and hospitals no longer meets modern requirements. Moreover, it is morally sound to postulate that all discovered means of alleviating suffering and sorrow, maintaining health and preventing death, should be freely available to all that need them—without reference to social, racial, or economic condition. This will demand a complete reorganization of practice, in which the medical profession must, and should, play the leading role; and undoubtedly it will—though there has been a tendency on the part of reformers, sociologists, government agencies, and professors of the teachers' union type to assume that reluctance to accept any and all proposals indicates a conservatism of self preservation based on purely venal motives. Let it not be forgotten that the situation as it now exists is entirely the consequence of the progress made in medical discovery by the profession itself; that the enhanced power for good which is now claimed as the latest of the inalienable rights of man is the result of the labors of medical investigators and practitioners, and that public health organization, social service, group practice, and all other advances which have revolutionized the relationship of medical knowledge to the population—even housing, nutrition, and the sociological conditions that influence health, such as wage scales, public parks, industrial hygiene, etc., etc.—were given their basis of factual observation and their early organization for practical application by the insight of medical men.
>
> There is in the practice of medicine a unique quality that is a source both of inspiration and of terror to the conscientious young physician. Dealing as it does with matters of life and death, any lack of knowledge or of skill becomes a positive fault of omission and even guilt. If a patient dies or is incapacitated—with all the heartbreak and suffering that this implies—because the attending practitioner was ignorant of measures that are available and that might have brought another outcome in more skilful hands, he is as responsible as though he had committed a wilful injury. This is true not only of surgical procedures, but equally—perhaps more frequently so—in infectious diseases, where speed and precision of diagnosis by well known methods and vigorous intelligent treatment may decide the issue within a few hours, one way or the other. It is this consideration, more than any other, which—with the growing accumulation of knowledge that no one man can hope to master completely—has automatically led to the organization of group medicine, the increasing cooperation of city and state health departments, and the more generalized utilization of hospital facilities. And since it is essential that all effective knowledge must be applied to rich and poor alike, unless our profession is to lose the fine, ancient traditions of its history, a considerable readjustment of its activities is inevitable. These simple considerations are at the bottom of all the agitation for the so-called "socialization" of medicine on which great volumes of reports have already been issued. It should not be forgotten, however, by the ardent lay reformers that evolution in these directions has long been going on within the profession itself, and, within a single span of professional life, enormous progress—almost entirely originated by public spirited doctors—has been achieved. Controversies have turned not at all on the objectives to be attained, but rather upon the manner in which the reorganization is to be carried out.

There are discussions of euthanasia with examples which make exceedingly clear the author's point of view. There are brief excursions in obstetrics, and many physicians will appreciate, as the result of his own experiences, the humor and insight which the author has for this part of the physician's occupations. Then comes the time when Zinsser becomes a great public citizen. You travel with him to Serbia, to Russia, to Africa and to the Far East, to Mexico and to France. You come at last to his chapter on "Philosophical Confusion," which is farewell to the present and his forecast for the future. He describes his own death. Where in literature is there to be found a contemplation of dissolution like the following?

> As his malady progressed, he had another variety of experience which, to some others more conditioned to religious belief than he was, might have signified an intimation of the separateness of body and soul.
>
> He said to me: "Here I am, me as always. My mind more alive and vivid than ever before; my sensitiveness keener; my affections stronger. I seem for the first time to see the world in clear perspective; I love people more deeply and more comprehensively; I seem to be just beginning to learn my business and see my work in its proper relationship to science as a whole; I seem to myself to have entered into a period of stronger feelings and saner understanding. And yet here am I—essentially unchanged except for a sort of distillation into a more concentrated me—held in a damaged body which will extinguish me with it when it dies. If it were a horse I was riding that went lame or broke its neck, or a ship on which I was traveling that sprang a leak, I could transfer to another one and leave the old vehicle behind. As it is, my mind and my spirit, my thoughts and my love, all that I really am, is inseparably tied up with the failing capacities of these outworn organs.
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> "Yet," he continued, apostrophizing in a seriocomic mood, "poor viscera, I can hardly blame you! You have done your best, and have served me better than could be expected of organs so abused. When I think of the things that have flowed over and through you! Innumerable varieties of fermented hops and malt and of the grapes of all countries and climates: Vouvray, Anjou, Chablis, Haut Sauternes, Chambertin, Nuits-Saint-Georges, Riesling, Lachryma Christi, Johannisthaler, Berncastler, Saint-Julien, Clos de Mouche, Liebfrauenmilch; endless amounts of pinard and vin du pays; the sour wines of Alsace, of North Africa, and of the Pyrenees; the stronger ones of Spain—Oporto, Sherry, Madeira, Malaga; the Tokay of Hungary; sparkling vintages of Burgundy and of Champagne; Veuve Cliquot and her brothers Mumm and Pommery; and the California brews bought in demijohns; to say nothing of the distillates—flavored and unflavored; cognac, Three-Star Hennessy; whiskeys—Scotch, Irish, Canadian, rye, bourbon, and the yellowish moonshine, colored with chicken droppings, from the Blue Hills; and gin—genuine and synthetic; Schlibovitz from the Balkans, Starka from Poland, and the vodka of the Steppes; crème de menthe and cacao, Marie Brizard, Cointreau, and Calvados.
>
> "No, no, my organs! I cannot feel that you have let me down. It is quite the other way round. Only now it seems so silly that you must take me with you when I am just beginning to get dry behind the ear."

Words fail to give any adequate picture of this exceptional book. Again the reviewer can only say that the physician who fails to read and to reread it again and again is depriving himself of some of the finest hours that literature can afford to a thoughtful man.

The Foot and Ankle: Their Injuries, Diseases, Deformities and Disabilities. By Philip Lewin, M.D., F.A.C.S., Associate Professor of Bone and Joint Surgery, Northwestern University Medical School, Chicago. Cloth. Price, $9. Pp. 620, with 303 illustrations. Philadelphia: Lea & Febiger, 1940

Here is a book filled to overrunning with a great deal of valuable and interesting information concerning the foot and the ankle. The author's first paragraph in the preface gives the key to the book: "The purpose of this book is to guide the student, general practitioner, industrial surgeon and younger orthopedic surgeon in the diagnosis and treatment of diseases, deformities and disabilities of the foot and ankle. It presents in natural sequence and concise language the underlying principles of etiology, pathology, diagnosis and treatment of congenital, static, infectious, paralytic and other lesions. Traumatic lesions including fractures, dislocations and industrial conditions are

given special attention. I endeavored at the outset to describe and illustrate everything that could happen to a human foot and ankle, but I soon found that it would make two volumes or one that was unwieldy."

A foreword by Dr. Michael Hoke, wherein he pays tribute to Dr. Lewin's efforts, is further made interesting by a hope that someday he (Hoke) may present in book form the full exposition of his thoughts on the subject. The medical profession would welcome such a book.

In another foreword Dr. Morris Fishbein calls attention to the fact that there is a tendency, with specialization, to detract considerably from attention to the body as a whole and to consider various organs and portions as if they were independent. Dr. Lewin has evidently been aware of this tendency, because he quotes the late Dr. W. J. Mayo as follows: "One cannot divide the patient into parts for repair as he can an automobile but must treat him as a human being, and the treatment given must be the best that the combined knowledge of science can afford."

The book is written in readable form and not in what might be called the jargon of the specialist. There are many descriptions of various valuable tricks of the orthopedic surgeon that the practitioner can just as well use and the author expresses the hope that his book "will make the mysteries of the foot and ankle an open book to the general practitioner."

The book is "dedicated to the memory of Dr. Allen B. Kanavel." Dr. Lewin says that in 1915 Dr. Kanavel said to him "Lewin, I wish, some day, you would do for the foot what I have tried for many years to do for the hand." Hence the book.

Considering the field, and the thoroughness with which Dr. Lewin has tried to cover it, there is little of a critical nature that can be fairly uttered. The book is of convenient size, the paper is good, the print is easily read and the illustrations are numerous. A few errors in referring to illustrations are to be noted and there are some repetitions, but these are minor faults. It might be said that too many methods of treatment are given and that the author fails to evaluate them. However, on careful reading, the author's preference is usually to be found. Perhaps he should have emphasized his own views a little more strongly. Also frequent references are made to opinions of others on controversial questions but in many instances no footnote or reference in the bibliography can be found to direct the reader to the original article. A complete bibliography, however, would greatly have increased the editorial work and one can always go to the *Quarterly Cumulative Index Medicus* if one is really interested. All in all, the book is well worthy of a place not only in the library of the specialist but also in that of the practitioner. The author is to be congratulated on an effort that has been well carried through to a result that will serve a useful purpose.

Transactions of the American Philosophical Society Held at Philadelphia for Promoting Useful Knowledge. New Series—Volume XXXI, Part II: Chronic Arthritis in Wild Mammals. By Herbert Fox, Professor of Comparative Pathology, University of Pennsylvania, Philadelphia. Paper. Price, $2. Pp. 73-149, with illustrations. Philadelphia, 1939.

Chronic arthritis stands high in the list of human ailments, and it incapacitates great numbers of people. Our knowledge of its nature and cause is lamentably inadequate. Studies in "comparative rheumatology," on how arthritis affects animals and whether such arthritis resembles the type which affects human beings might be supposed to throw some light on the problem. A few reports have been made on the disease as found in domestic animals but no reports have been made on its occurrence among wild animals.

Herein, Fox has reported results of an analysis of 1,749 skeletons and necropsies of animals. Some animals were captive specimens; many were wild animals killed in their natural environment. The material was from several institutions: the Philadelphia Zoological Garden; the Wistar Institute of Anatomy, Philadelphia; the National Museum, Washington; the Wagner Free Institute of Science, Philadelphia; Western Reserve University, Cleveland; the Academy of Natural Sciences, Philadelphia; the American Museum of Natural History, New York City. Among the great diversity of animals studied were seventy-seven whose skeletons showed definite arthritic changes. The articular lesions of the captive animals and of the wild animals were entirely comparable. These lesions were common among certain varieties, for example Felidae, Hyaenidae, Ursidae, Bovidae, Cervidae and especially anthropoid apes and baboons, rare or absent among certain Carnivora (Canidae) and among Rodentia (rats, mice, beavers, squirrels) and Chiroptera (bats).

Descriptions of the seventy-seven arthritic animals were given, based on studies of dried skeletons from museum or wet-cleaned bones at necropsy. These descriptions are amplified by more than sixty photographs of gross specimens and roentgenograms. The commonest lesion present was hypertrophic arthritis of the spine and was found in almost every case. Carnivorous animals exhibited "productive articular and periarticular disease" more often than did herbivorous animals; the latter more often presented "porotic and ulcerative articular lesions." Arthritis of extremities was noted in all varieties, but forelimbs were more affected in Carnivora, hind limbs in Artiodactyla. Contrary to the opinion of some that arthritis most often affects the most mobile portions of the spine (in human beings at least) Fox reported that in animals spondylitis occurs where the greatest stabilization of the spine is demanded for the animal's locomotion; that is, at the sites of greatest muscle rigidity or tonicity (sites of "osseomuscular fixation" or "stabilizing tension"). The presence of the arthritis was analyzed in relation to various other factors: the general body type, habits as to diet and "home life," age and associated morbid states. No relationship was found between the presence of the arthritis and zoogeography, ecology, individual habits, diet, associated diseases, and focal infection such as dental and alveolar disease. Finally, the author "cautiously suggested" that the hypertrophic or osteo-arthritic lesions of these animals were strongly similar to those of osteoarthritis of human beings and that certain lesions seen especially in gorillas resembled rheumatoid arthritis of human beings.

The material seems to have been carefully studied and the results are concisely presented. Although the work would appeal more strongly to the more serious students and specialists in rheumatic diseases, it can be read with benefit by practitioners. The author's comment regarding the apparent lack of relationship between diet or focal infection and the arthritis in animals would seem to withdraw support from certain current popular notions of treatment of arthritis in human beings.

The Electrocardiogram in Congenital Cardiac Disease: A Study of 109 Cases, 106 with Autopsy. By Maurice A. Schnitker, B.Sc., M.D., Associate Attending Physician, Toledo Hospital, Toledo, Ohio. Cloth. Price, $3. Pp. 147, with illustrations. Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1940.

The author has assembled 106 cases of congenital heart disease with electrocardiograms of his own and from the literature in which the congenital lesions were proved at necropsy. These cases are subdivided into several categories to determine the value of the electrocardiogram in such lesions. The results are summarized in the last chapter and it is concluded that most congenital lesions do not give a specific electrocardiographic curve. Group specificity was found only in congenital heart block, in dextrocardia with reversed chambers and in tricuspid valvular disease, particularly tricuspid stenosis. Usually it is impossible to tell from the electrocardiogram whether the heart has a congenital or an acquired cardiac defect. Among his conclusions are the following: A marked right ventricular preponderance suggests a congenital lesion; 36 per cent of the 106 cases assembled showed this. However, 21 per cent showed a left ventricular preponderance. Marked right ventricular preponderance is seen in cases with extreme narrowing of the pulmonary artery. When an associated appreciable defect in either septum is present, the right preponderance is less pronounced. Other lesions also give right ventricular preponderance, but its absence rules out any appreciable narrowing of the pulmonary artery or conus. The observations of Katz and Wachtel that biphasic QRS complexes of high amplitude in one or several leads occur in congenital heart disease is confirmed. This was found in thirty-two of the 106 cases studied post mortem. Such complexes are commonly associated with defects in either the auricular or the ventricular septum or in both. Auriculoventricular block and intraventricular block are often

also associated with a defect of either septum. High and pointed P waves are common with auricular septum defects but are seen in several other lesions causing auricular enlargement, such as pulmonic and tricuspid stenosis. Auricular fibrillation is also associated with enlargement of the auricles. Some of the electrocardiographic abnormalities occurring in congenital heart disease are due to the frequent presence of acquired rheumatic valvular disease and, in older patients, to other acquired cardiac disease. A downward direction of the major deflection of the QRS occurring in all three leads is found in congenital heart disease and is rare in acquired heart disease. Absence or atresia of the tricuspid orifice, aside from congenital lesions in the aorta, causes a marked left ventricular preponderance. This monograph, representing a painstaking assembly of proved cases of congenital heart disease, should be of value to physicians interested in the diagnosis of congenital heart disease.

Gerichtlich-medizinische und kriminalistische Blutuntersuchung: Ein Leitfaden für Studierende, Ärzte und Kriminalisten. Von Dr. med. Kurt Walcher, o. Professor, Vorstand des Instituts für gerichtliche und soziale Medizin der Universität Würzburg. Paper. Price, 12.60 marks. Pp. 175, with 50 illustrations. Berlin: Julius Springer, 1939.

The book deals with blood examination for medicolegal purposes. The methods and objectives are of course wholly different from the clinical. In the first part the methods and means of examining blood stains are described in detail from the first inspection of the suspected stain to the final demonstration of its kind, whether human or not, if it proves to be a blood stain. The illustrations of blood stains and tests are instructive. In the discussion of the differences between maternal and fetal blood no mention is made of the fact that fetal blood contains more or less hemoglobin antigenically and otherwise different from adult hemoglobin. The second part is concerned with the technic of blood grouping for court purposes, including the grouping of dried blood and blood from cadavers. The third part describes the determination of the alcohol content of the circulating blood as practiced particularly in connection with automobile accidents. It appears that at present Widmark's method is used exclusively in Germany. This is a book that will interest those who are concerned with blood in its forensic aspects.

Ascorbinsäurestudien an Gesunden und Tuberkulosekranken. Von H. Dagulf. Paper. Pp. 195, with 26 illustrations. Göteborg: Elanders Boktryckeri Aktiebolag, 1939.

The author presents in this monograph an account of investigations made in the Küstensanatorium Apelviken, Varberg, on the importance of vitamin C in the treatment of tuberculosis. He studied various methods of determining vitamin C deficiency, such as the capillary resistance test and various chemical methods for the estimation of ascorbic acid in the blood serum and in the urine. The amount of reduced ascorbic acid in the blood serum is a significant index of the condition of the patient. In 326 healthy persons an average value of 0.22 mg. of ascorbic acid per hundred cubic centimeters of serum was found early in the year and 0.90 mg. per hundred cubic centimeters of blood serum in late summer. In 225 tuberculous patients the values were less, being 0.10 and 0.48 mg. per hundred cubic centimeters of blood serum respectively. It was concluded from these studies that a tuberculous patient needs about three times as much vitamin C as a healthy person.

Manual of Urology. By R. M. LeComte, M.D., F.A.C.S., Professor of Urology, Georgetown University, Washington, D. C. Second edition. Cloth. Price, $4. Pp. 295, with 55 illustrations. Baltimore: William Wood & Company, 1939.

This manual deals in a practical and concise manner with the diseases of the genito-urinary tract. The subject matter is systematically arranged and the author presents each chapter in the same way, stressing especially the etiology of various conditions. He avoids extended discussions and case reports and, as a rule, presents generally recognized conclusions. The importance of obtaining a careful history is given due consideration and the question of a physical examination in urologic conditions is given in detail. The newer concepts of the neuromuscular physiology of the bladder has been added. The subject of prostatic obstruction is presented, including an adequate discussion of suprapubic prostatectomy, perineal prostatectomy and transurethral resection. A chapter has been added on impotence and sterility. Although he realizes that much of our present day point of view is subject to discussion and that these views may change, the subject is presented in a comprehensive, simple, straightforward way. This book may well serve the busy practitioner as a handy reference work as well as serving the student, who so many times is pressed for time.

The Displacement Method of Sinus Diagnosis and Treatment. By Arthur W. Proetz, A.B., M.D., Professor of Clinical Otolarynogology in the Washington University School of Medicine, St. Louis. Second edition. Cloth. Price, $6. Pp. 296, with 157 illustrations. St. Louis: Annals Publishing Company, 1939.

From a theoretical and practical point of view, this work is a landmark. It won the Casselberry Prize of the American Laryngological Association in 1931. Few have done as much as the author to clarify the physiologic mechanism of the mucosa of the nose and accessory nasal sinuses. The more rational therapy of today depends in large part on Proetz's work. He investigated the physiologic anatomy of the lining membrane of the sinuses, their ostia, the ciliary behavior and the effects of ventilation and drainage on the air chambers. This work is a summation of his researches and since its first publication in 1931 has had a definite influence for good on the diagnosis and treatment of suppurative disease in the nasal accessory sinuses. The diagnostic role of radiopaque oils and the treatment of sinus disease by the author's method of displacement are not among the least of his contributions to our knowledge. The present edition, as the author indicates, remains in large part unchanged over the first one. There have been added illustrations and also comment from the literature on experience gained and practical deductions arrived at by numerous persons over the past few years.

Diathermie chirurgicale. Par le Docteur C.-A. Arraud, assistant de physiothérapie à l'Hôtel-Dieu. Les actualités physiothérapiques. 1: Électrothérapie, 7. Publiées sous la direction du Dr Duhem. Paper. Price, 50 francs. Pp. 216, with 52 illustrations. Paris: Gauthier-Villars, 1939.

This is an excellent manual on surgical diathermy. Starting with a section on history, the text continues with a discussion of the employment of electrocoagulation, fulguration and the cutting current. Various types of apparatus are carefully described and there are many excellent line drawings of these devices. A clinical section follows in which there is detailed description of the employment of surgical diathermy in the treatment of cancer, in diseases of the skin and appendages, in gynecology, in urology, in lesions of the digestive tract and in lesions of the brain, pleura and lungs. There are also sections on surgical diathermy in otorhinolaryngology and ophthalmology. The entire book is well organized, the material is systematically presented and throughout the illustrations of apparatus are clear and understandable. The author falls into a common error when he writes of the application of high frequency currents as bipolar and monopolar. As a matter of fact the high frequency current possesses no polarity. Instead of using the terms "bipolar" and "monopolar," the designations "biterminal" and "monoterminal" should have been employed. Although the author describes the devices of many surgeons, there is no list of references and unfortunately there is no index. Aside from these few shortcomings the text is well prepared and readily understandable. It is recommended to any surgeon or physician who is interested in this important and somewhat neglected field and who reads French.

Illustrations of Surgical Treatment, Instruments and Appliances. By Eric L. Farquharson, M.D., F.R.C.S.E., Tutor in Clinical Surgery, Royal Infirmary of Edinburgh, Edinburgh. With a foreword by Sir John Fraser, M.C., M.D., Ch.M., Regius Professor of Clinical Surgery, University of Edinburgh. Cloth. Price, $6.50. Pp. 338, with 316 illustrations. Baltimore: William Wood & Company, 1939.

The author is generally correct in his assumption that too many textbooks of surgery and orthopedics subordinate illustrations of treatment to those of clinical conditions and pathologic specimens. His book fills this need admirably as far as the treatment of fractures and certain of the commoner orthopedic conditions is concerned. The student and intern who have read this book will have a much better understanding of the use of splints and other mechanical devices in the treat-

ment of these conditions, and there are many practical devices and methods that should prove valuable to the practicing surgeon. For purposes of review the book may be divided into three parts. The sections on intravenous infusion and blood transfusion are very brief. Much of the blood transfusion apparatus illustrated is being rapidly replaced by sealed containers and vacuum bottles in this country. No mention is made of the various types of direct blood transfusion apparatus. The largest portion of the book is devoted to the treatment of injuries, fractures, dislocations and such orthopedic conditions as tuberculosis of the spine and foot deformities. This is profusely illustrated with excellent photographs and sketches. The text is concise, clear and inclusive. Mechanisms of fractures are briefly discussed. The purposes and reasons for the use of various devices are given. After-treatment is not neglected. The ingenuity of the author is evident throughout. The third section of the book is devoted to illustrations of surgical instruments and is included to facilitate demonstrations to students. The surgeon will gain little from it.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Liability for Incorrectly Diagnosing and Treating Infection of Jaw as Trigeminal Neuralgia.—The defendant physicians as partners operate a clinic. On Feb. 15, 1937, Sinclair consulted defendant Haven at the clinic because of pain in his face and upper jaw on the right side. After taking a history of the case, making a physical examination, causing roentgenograms to be taken and carrying out certain laboratory tests, Dr. Haven diagnosed Sinclair's condition as a trifacial or trigeminal neuralgia. Two days later he resected the posterior root of the trigeminal nerve which he believed was causing the trouble. As the pain was not relieved, on February 26 he performed a second operation and apparently resected an additional portion of the nerve. According to the published report, a paralysis of one side of Sinclair's face resulted from these operations "with the loss, on that side, of all teeth and of the sense of taste, a gradual loss of hearing and eyesight, and the distortion of the face to such an extent as to render the features repulsive." The pain still persisted and on March 15 Sinclair consulted another physician, Dr. Wanamaker, who had formerly practiced dentistry. Dr. Wanamaker, after taking roentgenograms, found that the sole cause of Sinclair's suffering was an infection of the upper jaw in the region of the socket of a tooth that had been extracted in the autumn of 1936. He made an incision in this area, extracted two teeth and, finding the bone spongy, "scraped some of the jaw bone out." Thereafter Sinclair improved. Later he sued the defendants, alleging that the severance of his trigeminal nerve was unnecessary and had resulted from defendant Haven's negligence in failing to keep him under observation for a sufficient length of time and in failing to make any tests in advance of the operation to determine the real cause of his condition. From a judgment in favor of Sinclair, the defendants appealed to the Supreme Court of Washington.

At the trial Sinclair testified that he began to have intermittent pain in his face and upper jaw on the right side in 1934 but that it was not until after the extraction of his right upper third molar in 1936 that the pain became severe and would appear suddenly. Dr. Haven, however, testified that this story differed from the case histories which he and his assistant independently elicited from Sinclair and that if he had obtained such information he would have asked additional questions, made other investigations and made a different diagnosis and would not have advised operation unless "there were trigger zones obvious there." He claimed that before he operated he examined Sinclair's gum in the region of the socket of the extracted tooth. He further testified that, although the motor branch of the trigeminal nerve is not readily distinguished and is not easily separated from the sensory fibers causing most surgeons to pay little attention to it, he had always tried to avoid injuring that branch but nevertheless in the course of the operations on Sinclair he had injured it. A partner of Dr. Haven testified that roentgenograms taken on the day Sinclair entered the clinic showed an "infected condition in the jaw" and that he had informed Dr. Haven of that fact either that day or the next morning, "probably before he operated." Dr. Haven could not recall whether the roentgenograms were examined by him before he advised Sinclair that an operation was necessary. Dr. Wanamaker, who was called as a witness for the defendants, testified that a careful examination of the teeth is usually made before a diagnosis of trigeminal neuralgia is made and that the roentgenograms taken at the clinic showed that Sinclair had a "tooth infection." Another medical witness for the defendants, a surgeon, testified that if roentgenograms showed an infected area he would probably send the patient to a dentist before operating.

The plaintiff, said the Supreme Court, based his claim for recovery solely on the basis of a negligent diagnosis made by defendant Haven. It is well settled that when a physician takes charge of a case a duty is imposed on him by law to possess and exercise reasonable skill and learning, that is, such skill and learning as is possessed by the ordinary practitioner in the general locality, measured by the state of medical science at that time. He is not negligent merely because the result is not what was desired. After reviewing the evidence the court could find no justification for disturbing the finding of the jury, in effect, that Sinclair had not been suffering from trigeminal neuralgia. If the evidence in a case is conflicting, on appeal the court must assume as true that version of the case which tends to support the jury's verdict. In the judgment of the court, the testimony in the instant case clearly raised an issue of fact whether defendant Haven had failed to exercise due care before making his diagnosis of trigeminal neuralgia, and so the trial court properly denied the defendants' motion for a directed verdict and for judgment notwithstanding the verdict. The court was also of the opinion that, contrary to the contention of defendant Haven, a qualified dentist who had been called as a witness by the plaintiff was competent to testify as to the difference between pain caused by "tooth conditions" as might be revealed by roentgenograms and pain characteristic of trigeminal neuralgia.

For the reasons just stated, the judgment in favor of the plaintiff was affirmed.—*Sinclair v. Haven et al. (Wash.), 89 P. (2d) 820.*

Society Proceedings

COMING MEETINGS

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Excelsior Springs, Mo., Sept. 26-28. Dr. James R. Bloss, 418 Eleventh St., Huntington, W. Va., Secretary.

American Association of Railway Surgeons, Chicago, Sept. 16-18. Dr. Daniel B. Moss, 547 West Jackson Blvd., Chicago, Secretary.

American Congress of Physical Therapy, Cleveland, Sept. 2-6. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.

American Hospital Association, Boston, Sept. 16-20. Dr. Bert W. Caldwell, 18 East Division St., Chicago, Executive Secretary.

American Roentgen Ray Society, Boston, Sept. 26-Oct. 4. Dr. Carleton B. Peirce, Royal Victoria Hospital, Montreal, Canada, Secretary.

Colorado State Medical Society, Glenwood Springs, Sept. 11-14. Mr. Harvey T. Sethman, 537 Republic Bldg., Denver, Executive Secretary.

Idaho State Medical Association, Sun Valley, Sept. 11-14. Dr. J. N. Davis, 204 Fourth Ave., East, Twin Falls, Secretary.

Kentucky State Medical Association, Lexington, Sept. 16-19. Dr. A. T. McCormack, 620 South Third St., Louisville, Secretary.

Michigan State Medical Society, Detroit, Sept. 24-27. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing, Secretary.

Mississippi Valley Medical Society, Rock Island, Ill., Sept. 25-27. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

National Medical Association, Houston, Tex., Aug. 12-16. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.

Oregon State Medical Society, Eugene, Sept. 4-7. Dr. Morris L. Bridgeman, 1020 S.W. Taylor St., Portland, Secretary.

Pennsylvania, Medical Society of the State of, Philadelphia, Sept. 30-Oct. 3. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh, Secretary.

Utah State Medical Association, Ogden, Aug. 29-31. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.

Washington State Medical Association, Tacoma, Aug. 26-28. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.

Wisconsin, State Medical Society of, Milwaukee, Sept. 18-20. Mr. J. G. Crownhart, 110 East Main St., Madison, Secretary.

Wyoming State Medical Society, Sheridan, Aug. 11-13. Dr. M. C. Keith, State Department of Health, Cheyenne, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

9:409-488 (June) 1940

Evaluation of Various Gonadotropins: Their Application to Female Endocrine Disorders. R. B. Greenblatt and R. Torpin, Augusta, Ga. —p. 409.

Intestinal Obstruction. W. C. Kennedy, Florence.—p. 415.

The Philosophy of Sound Public Health Organization. J. N. Baker, Montgomery.—p. 416.

Dental Caries in Children: Responsibility of Dentist and Physician. J. F. Alison, Selma.—p. 420.

American J. Digestive Diseases, Huntington, Ind.

7:227-276 (June) 1940

Contributions Made in 1939 to Knowledge in Regard to the Pancreas. R. Elman, St. Louis.—p. 227.

Calcification of Pancreas. C. A. Beling, South Orange, N. J.—p. 231.

Ulcerative Colitis. C. J. Donald and P. W. Brown, Rochester, Minn.—p. 234.

Allergy of Gallbladder: Study Using Graham-Cole Test and Leukopenic Index. H. Necheles, B. Z. Rappaport, R. Green, P. Marcus and S. Mesirow, Chicago.—p. 238.

*Gastroscopic Inspection of Pylorus. R. Schindler, Chicago, and F. Hernandez Morales, San Juan, Puerto Rico.—p. 242.

Improved Routine for Roentgen Examination of Rectum and Sigmoid. W. H. Stewart, F. Huber and F. H. Ghiselin, New York.—p. 244.

Influence of Raw Banana and Apple on Disappearance of Complex Carbohydrates from Alimentary Tracts of Normal Children. Marion L. Shepherd, Frances Cope Hummel and Icie G. Macy, with assistance of Helen A. Hunscher, Mary Bates Olson, Louise Emerson and Theresa A. Johnston, Detroit.—p. 248.

Dysphagia Ascribed to Vitamin B Deficiency. I. R. Jankelson, Boston. —p. 252.

Gastroscopic Inspection of Pylorus.—Schindler and Morales believe that proper technic and good training can improve the reported 60 to 70 per cent of cases in which the pylorus is seen on examination with the flexible gastroscope. In 313 new gastroscopic examinations they visualized the pylorus in 285, or 91.1 per cent. They do not claim that this figure is the best that can be attained but believe that the gastroscopic technic cannot be considered adequate if the pylorus is not observed in at least 80 per cent of all cases in which pathologic conditions do not exist which prevent it from being viewed. This result can be attained only by adequate technic. The most essential point is to avoid gastric spasm. This is accomplished by a good psychologic preparation of the patient and by skilful introduction of the gastroscope. The chief technical point concerns the speed of the introduction. The constrictor muscle of the pharynx should be passed slowly while the patient is swallowing. After this passage not more than from one to three seconds should elapse in introducing the tip of the instrument down to the lower depths of the organ. No danger or resistance is involved in this rapid procedure and no spasm develops. On the contrary, slow introduction may cause severe spasm and poor results will be obtained. If spasm should develop, the patient's attention should be diverted and the spasm released before examination is attempted. This can be done only by talking continuously, not advising the patient to relax but describing the picture obtained or seen to the assistant or the observers. The patient will become interested and all his tenseness will disappear, the spasm will be gone and the instrument will slide down into the lower depths of the stomach. When the antrum is located, the pylorus is usually easy to see if the examiner is patient and waits until the antrum springs into action. The contractions of the antrum are frequently seen immediately but at times one has to wait for several minutes before they start. These few minutes will be almost unbearable to the patient if his attention is not constantly diverted by a concise, comprehensive and emphatic description of the picture observed. Faulty technic may discredit the endoscopic examination of the stomach with the flexible gastroscope.

American Journal of Psychiatry, New York

96:1263-1514 (May) 1940. **Partial Index**

Preliminary Analysis of Grouping Behavior in Patients with Cerebral Injury by Method of Equivalent and Nonequivalent Stimuli. W. C. Halstead, Chicago.—p. 1263.

Syphilis in Serum Negative Feebleminded Children: Histologic Study in Meningo-Encephalitis Syphilitica and in Nissl-Alzheimer Endarteritis. C. E. Benda, Wrentham, Mass.—p. 1295.

Tuberculosis Prevention and Treatment in Ontario Mental Hospitals. C. A. Wicks, Toronto.—p. 1335.

Note on Uselessness of Analeptic Drugs Combined with Luminal in Treatment of Epilepsy. T. T. Stone, I. Finkelman and A. J. Arieff, Chicago.—p. 1377.

Psychoses Resembling Schizophrenia Occurring with Emotional Stress and Ending in Recovery. H. A. Paskind and M. Brown, Chicago. —p. 1379.

Effect of Metrazol Administration on Prolonged Refusal of Food in Psychoses. S. Androp, Catonsville, Md.—p. 1407.

Mechanism of Fractures of Vertebral Bodies: Fractures of Midthoracic Area Complicating Metrazol Therapy—Prevention and Treatment. A. M. Rechtman, Philadelphia.—p. 1429.

Mutism and Resistance Behavior in Psychotic Patients: Physiologic Study. C. W. Darrow and A. P. Solomon, Chicago.—p. 1441.

Metrazol as Diagnostic Aid in Epilepsy. H. H. Goldstein and J. Weinberg, Chicago.—p. 1455.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

43:805-958 (June) 1940. **Partial Index**

Clinical Consideration of Stomach. G. H. Laing, Chicago.—p. 805.

Forms of Ulcerative Colitis: Correlation of Clinical and Roentgenologic Data. H. M. Weber and J. A. Bargen, Rochester, Minn.—p. 809.

*Surgical Treatment of Ulcerating Gastric Lesions with Correlated Roentgenologic Studies. W. Walters, Rochester, Minn.—p. 819.

Differential Diagnosis of Pyloric and Prepyloric Ulceration. H. P. Doub, Detroit.—p. 826.

Aneurysms of Ascending Aorta, Aortic Arch and Innominate Artery: Clinical, Anatomic and Roentgenologic Study. C. F. Nichols, H. W. Ostrum and B. P. Widmann, Philadelphia.—p. 845.

*Irradiation of Long Bones for Gynecologic Bleeding. J. S. Bouslog and J. R. Evans, Denver.—p. 871.

*Postirradiation Changes in Lungs and Thorax: Clinical, Roentgenologic and Pathologic Study, with Emphasis on Late and Terminal Stages. J. R. Freid and H. Goldberg, New York.—p. 877.

Effect of Visible Light on Development of Tumors Induced by Benzpyrene in Skin of Mice. J. J. Morton, Ethel M. Luce-Clausen and E. B. Mahoney, Rochester, N. Y.—p. 896.

Further Studies on Action of Roentgen Rays on Gametes of Arbacia Punctulata: Parts I to VI. P. S. Henshaw, Bethesda, Md., and I. Cohen, New York.—p. 899.

Ulcerating Gastric Lesions.—Walters states that roentgenologic examination of the stomach, supplemented by gastroscopic examination, will serve to decrease to a minimum the error in the diagnosis of intragastric lesions. Since the history of many patients who have carcinoma of the stomach in the early stages suggests peptic ulcer, such patients should not be assumed to have benign lesions of the stomach or duodenum until this is proved by x-ray examination and the presence of an intragastric malignant lesion is excluded. An occasional malignant gastric ulcer will produce sufficient pylorospasm to lead to the erroneous assumption that the lesion is in the duodenum and is benign, when in reality it is in the stomach and may be malignant. The possibility of this error should always be borne in mind. Gastroscopic examination is of great assistance in localizing or excluding the lesion. The roentgenologist's report that a gastric ulcer is malignant is practically always correct, but the report that a gastric ulcer is present and that it is benign does not exclude its being malignant. Evidence seems to indicate that the percentage of gastric ulcers that are malignant as well as the number of malignant lesions which start as gastric ulcers is much nearer 20 than 10 per cent. Roentgenologic examinations of the stomach and colon of patients who have anemia have frequently shown that a bleeding polyp is its cause. Many of these polyps contain malignant cells in their periphery, and their early recognition and removal may prevent the development of an extensive malignant lesion. Roentgenologists can demonstrate polypoid lesions of this type that are as small as 0.5 cm. in diameter.

Irradiation of Long Bones for Gynecologic Bleeding.—Bouslog and Evans encountered cases of functional uterine bleeding, intractable to ordinary forms of treatment, in which

the only positive abnormal finding was a decreased platelet count. Because there were no other symptoms of purpura, the authors assumed that the diminution of platelets was due to a deficient formation in the bone marrow rather than to increased destruction by the reticulo-endothelial system (primarily the spleen). Therefore irradiation of the long bones (100 roentgens to each of the long bones on several occasions) was instituted and the results were immediately successful: the bleeding ceased when the platelet count returned to normal. The disorder has been designated uterine purpura. The factors for irradiation were 200 kilovolts, 50 cm. distance, 0.5 or 0.75 mm. of copper and 1 mm. of aluminum filtration and a field of from 4 to 10 by 10 to 20 inches, focusing over the middle of each femur, fibula and tibia.

Postirradiation Changes in Lungs and Thorax.—Freid and Goldberg studied eighteen cases for twelve years after radiation to the thorax for malignant lesions. Among the late manifestations is the terminal picture of severe pulmonary fibrosis associated with signs of failure of the right side of the heart. There were eleven fatalities, and postmortem studies were made on eight. X-ray studies in the early stages of reaction revealed pulmonary inflammation followed by irregular patches of consolidation radiating out from the hilus. When the irradiated fields are large, concomitant pulmonary and pleural reactions are the rule. Adhesions occur between the pleura and pericardium and between the diaphragm and pericardium or pleura, with tenting of the medial portion of the diaphragm. If no further treatment is given and if the initial course has not produced extensive injury, the sole residue months later may be slight pulmonary fibrosis and a few pleural, pericardial and diaphragmatic adhesions. Atelectasis is common in the area of irradiation, with compensatory emphysema in the noninvolved portions. The diaphragm shows numerous pleural and pericardial adhesions, resulting in tenting and some elevation. The heart and trachea are drawn over to the involved side. The thorax, as a rule, becomes contracted. With the passage of years, fairly large and sharply outlined calcific plaques may appear in the irradiated lung or pleura, in addition to the fibrosis. Patients with lung damage of any extent show cutaneous damage, telangiectasia, slight atrophy and brawny induration. The area of pulmonary involvement corresponds to the area of cutaneous damage. Rarefying osteitis in the field of irradiation occurs in patients surviving for long periods. Fractures are common in the irradiated ribs or clavicle. The earliest clinical signs are cough, usually nonproductive and at times paroxysmal, slight dyspnea and chest pain at the area treated. Fever and sweating may also occur. If the damage is limited, these symptoms disappear when the pneumonitis resolves. When the pulmonary damage is marked by fibrosis the cough is persistent, the dyspnea progressive and the chest pain severe. Severe cases progress to a terminal stage when the symptoms are predominantly those of failure of the right side of the heart. The postmortem examinations on the eight patients were made from six weeks to eight years following irradiation. Macroscopically the irradiated portions of the lungs were atelectatic and firm, and they cut with increased resistance, showing obliteration of normal markings. Injection of the pleura, fibrinous deposits and extreme thickening were observed. Microscopically, when the irradiation was of long duration, severe fibrosis, hyalinization, dilatation of the bronchi, bronchiectasis and bronchitis were observed. Persisting alveoli were small and frequently filled with inflammatory exudate. Areas of edema, hemorrhage and necrosis were observed in the acute cases. Atherosclerosis of the pulmonary arteries, thickening, edema and thrombosis of the pulmonary vessels, and thrombosis of the inferior pulmonary artery were present. Hypertrophy or dilatation of the right side of the heart was present in six cases; the two cases that did not show this were acute and death occurred two months after the pneumonitis. Pericarditis, pericardial effusions and parietal pericardial adhesions were observed in four instances. The authors believe the following points will be of value in preventing damage: 1. The lung damage will appear under the portion of the chest wall that is most heavily irradiated and when cross-firing is used. 2. Massive single doses are likely to produce such injuries. 3. Irradiation limited to the lung periphery is less likely to produce serious injury than that over the mediastinum and large vessels. 4. Previous therapy with no injury can be the basis for later damage with subsequent treatment. 5. If some pneumonitis results from primary therapy, additional irradiation may cause severe damage. 6. Elderly individuals with arteriosclerotic changes must be considered more likely to have such damage. 7. Pulmonary metastases must be accepted with reservation when heavy dosage has been given. 8. Roentgenograms taken during and following treatment will call attention to pulmonary damage in its incipient stages and will help differentiate it from metastases.

Archives of Otolaryngology, Chicago

31:885-1050 (June) 1940

Otomycosis: Treatment with Silver Picrate. M. O. Dart, Denver. —p. 885.
Elongated Styloid Process: Cause of Obscure Throat Symptoms. M. Fritz, Durham, N. C.—p. 911.
Pyogenic Granuloma of Nasal Fossa. I. Frank and Margery Blahd, Chicago.—p. 919.
Treatment of Chronic Hypertrophic Laryngitis. F. J. Putney and L. H. Clerf, Philadelphia.—p. 925.
The Canine Fossa. W. J. Mellinger, Santa Barbara, Calif.—p. 930.
Pseudoxanthomatous Tumor of Mastoid: Résumé of Lipoidoses. C. H. McCaskey, Indianapolis.—p. 938.
Cavernous Sinus Thrombosis: Report of Recovery Following Sulfapyridine Therapy. L. F. Morrison and M. Schindler, San Francisco. —p. 948.
Simplified Technic for Construction of Life Masks of Latex Rubber. S. Peluse, Los Angeles.—p. 955.
Peroral Endoscopy. L. H. Clerf and F. J. Putney, Philadelphia.—p. 979.

Archives of Pathology, Chicago

30:1-464 (July) 1940. **Partial Index**

Rheumatic Disease of Tricuspid Valve. M. D. Altschule and E. Budnitz, Boston.—p. 7.
Renal Lesions Associated with Deep Jaundice, with Comments on Their Relations to Those in So-Called Hepatorenal Syndrome and in Transfusion Reactions. D. Ayer, Boston.—p. 26.
Subcutaneous Nodules of Rheumatoid Arthritis and Rheumatic Fever: Pathologic Study. G. A. Bennett, J. W. Zeller and W. Bauer, Boston. —p. 70.
Healed Pulmonary Infarcts. B. Castleman, Boston.—p. 130.
Myo-Epithelial Hamartoma of Gastrointestinal Tract: Report of Eight Cases with Comment Concerning Genesis and Nomenclature. B. E. Clarke, Providence, R. I.—p. 143.
Neuropathic Pulmonary Edema: Further Observations. S. Farber, Boston.—p. 180.
Meningioma. N. C. Foot, New York.—p. 198.
Immunity to Fowlpox Studied by Means of Skin Grafts on Chorio-Allantois of Chick Embryo. E. W. Goodpasture and Katherine Anderson, Nashville, Tenn.—p. 212.
Lead Absorption and Intoxication in Man Unassociated with Occupations or Industrial Hazards: Absorption of Lead from Eleven Weeks of Intra-Uterine Life to Ninety-Three Years of Age. G. H. Hansmann and M. C. Perry, Milwaukee.—p. 226.
Genesis of Hydatidiform Mole. A. T. Hertig and H. W. Edmonds, Boston.—p. 260.
Visceral Lesions Associated with Varicella. H. N. Johnson, Montgomery, Ala.—p. 292.
Carcinoma in Situ of Stomach and Its Bearing on Histogenesis of Malignant Ulcers. T. B. Mallory, Boston.—p. 348.
Mechanism of Leukocytosis with Inflammation: Nature of Leukocytosis-Promoting Factor in Exudates. V. Menkin, Boston.—p. 363.
Toxoplasma Infection in Man. H. Pinkerton and D. Weinman, St. Louis.—p. 374.
Primary Carcinoma in the Negro: Anatomic Distribution of 300 Cases. W. S. Quinland and J. R. Cuff, Nashville, Tenn.—p. 393.
*Pathologic Changes Observed in Human Tissues Subjected to Subcritical Temperatures. L. W. Smith, Philadelphia.—p. 424.
*Radiation Pneumonitis: Experimental and Pathologic Observations. S. Warren and Olive Gates, Boston.—p. 440.

Changes in Tissues Subjected to Subcritical Temperatures.—Smith describes the microscopic changes of more than 100 cancers in the terminal stages subjected to local application of cold and/or reduction of body temperature. Although the cancerous processes had gone on to their anticipated fatal outcome, it is the author's impression that in the majority of instances life has been prolonged beyond the period of expectancy and that death was a much less terrible ordeal because pain was controlled. Some sixty general necropsy specimens (designated as normal tissues), serial biopsy specimens from accessible tumor masses subjected to local cold (from 40 to 50 F.) and metastatic tumor tissues were studied. Prolonged subjection of normal adult differentiated cells to levels of temperature critical for embryonal cells is without significant effect. Neither gross nor microscopic evidence was found to indicate that such normal cells are influenced in any way even when subjected to almost constant local temperatures of from 40 to 50 F. for as long as five months. Indeed, healing was seen to

go on uninterruptedly at these levels in a number of ulcerative lesions. Complications producing changes of pathologic significance to the subject as a biologic unit were seen in five instances in which refrigeration was accompanied by unexplained myocardial failure. The possibility of terminal bronchopneumonia as a complication following reduced body temperatures must be recognized in cases of terminal malignant conditions of the lungs associated with cachexia and anemia. Whether its incidence is significantly different from that of terminal pneumonia in similar cases not subjected to reduced body temperatures seems extremely doubtful. The cell changes in tumors subjected to local temperatures of from 40 to 50 F. were generally regressive, even to the point of microscopic clearance of the tissue of tumor cells in occasional instances. Granular, hydropic and fatty degenerative changes were observed in the cytoplasm of the cells. The more undifferentiated the tumor cells were, especially if they belonged to the epithelial series, the more rapid and extensive were the regressive phenomena. Microscopically the effects of cold are not unlike the effects of roentgen irradiation. These merely represent physical agents occurring at different points on the physical spectrum, and the hypothesis is again advanced that, through the withdrawal of the heat stimulus of cell growth by the application of cold, tumor tissue may well be rendered more susceptible to the harmful wavelengths of the x-rays, radium or other as yet undiscovered rays. The changes in metastatic tumor tissue of patients submitted to general reductions of temperature to from 74 to 90 F. were similar in kind but varied greatly in degree to those resulting from low temperatures applied locally. Regressive changes were not encountered until from ninety-six to 120 hours of refrigeration had been given, and in some cases no significant change seemed to occur even after 300 hours of such low temperatures.

Radiation Pneumonitis.—Warren and Gates studied the early effects of roentgen, radon and radioactive phosphorus irradiation of the lungs of normal animals of different species, correlating them with observations on irradiated human lungs. The present study confirms, clarifies and extends the criteria for radiation pneumonitis used by Warren and Spencer (1938). The progression of the response to irradiation has been followed up to a stage in the reaction which has been observed with considerable constancy in man. Congestion, edema, exudation and tissue injury (epithelial and mesenchymal) occur in different combinations. In a series of rats in which from 30 to 159 microcuries of radioactive phosphorus was injected, congestion and edema with focal hemorrhages, but no cellular exudation, appeared after twenty-four hours and during the next few days were overshadowed by proliferation and swelling of the alveolar lining cells as well as by polymorphonuclear infiltration. Mitosis in alveolar cells was frequent on the fifth and sixth days after injection. Irregularity in the bronchial mucosa appeared about the third day, and by the seventh day considerable anaplasia developed gradually. Degeneration of the elastica is probably important in producing emphysema in irradiated lungs. The cough and respiratory difficulty commonly present in human radiation pneumonitis may be due to increased bronchial secretion, impairment of ciliary function and edema. These in turn may produce atelectasis, aggravate emphysema and lead to infection. These early changes produce distinct clouding of the lung fields on x-ray examination, and, if not too severe, complete restoration is possible. It is not known whether the hyaline membrane is eventually autolyzed. The authors have never seen evidence of its organization. They are in accord with most observers with regard to the importance of congestion, edema, petechial hemorrhage and lymphangiectasia as early and constant elements in the reaction. However, they have not seen the pigmentation, presumably hemosiderin, described so often. The tendency in the literature has been to emphasize fibrosis, inflammation and pleural change, overlooking the less striking and often obscured underlying changes. The authors attribute absence of fibrosis in their animals to the doses and spacing of radiation and to the absence of any considerable inflammation. Severe injury of the tissues following the use of radiation probably increases their susceptibility to infection. Some clinical and experimental evidence indicates that inflammation of the lung, as of the skin, may render the tissues more sensitive to radiation. Extensive fibrous and pleural adhesions occur only as a result of actual pleural necrosis or inflammatory reaction. Such pulmonary reactions may well be secondary to bronchial epithelial change and loss of cilia due to the effect of radiation. The authors believe that the constant displacement in human patients of the mediastinum toward the affected lung is not so much the result of adhesions or "traction" as of atelectasis. In one other respect their observations differed from those previously described, the degeneration of the elastica of the alveoli, pleura and vessels occurring with any well established reaction. The experimental data suggest that the reaction of the lungs to radiation need not be a hazard in therapy provided the potential danger is realized and signs or reactions are looked for.

Archives of Physical Therapy, Chicago

21:321-384 (June) 1940

Role of Exercise in Cardiac Disease and Edema. A. A. Sussman, Baltimore.—p. 325.
Raising of Venous Pressure in Surgical Shock by Faradic Stimulation. G. G. Ornstein, S. Licht and M. Herman, New York.—p. 329.
Autohemotherapy Combined with Artificial Fever: Further Observations in Treatment of Rheumatic Disease. W. K. Ishmael, Oklahoma City.—p. 335.
Treatment of Atrophic Arthritis with Artificial Fever Therapy. W. M. Solomon and R. M. Stecher, Cleveland.—p. 339.
Short Wave Diathermy of Carotid Sinus. A. B. Hertzman, W. F. Alexander and A. J. Kotkis, St. Louis.—p. 348.
Method of Comparative Climatologic Investigations. G. Cronheim, Saratoga Springs, N. Y.—p. 353.
Point Heating and Mechanical Effects of Short Waves. W. Krasny-Ergen, Stockholm, Sweden.—p. 362.

Connecticut State Medical Journal, Hartford

4:311-376 (June) 1940

Trichinosis. G. Blumer, New Haven.—p. 314.
The American Medical Association—New Haven—1860. C. Barker, New Haven.—p. 319.
American Federation of Labor and Health Insurance. R. J. Watt, Washington, D. C.—p. 322.
Obstetric Aspects of Prematurity. E. L. Stone, New Haven.—p. 326.
Digitalis U. S. P. XI: Recent Changes in Potency and Designation. A. J. Geiger, New Haven.—p. 331.
Treatment of Gonococcic Salpingitis and Arthritis with Sulfanilamide. R. M. Lewis, New Haven.—p. 335.
Pneumomyelography in Diagnosis of Spinal Cord Lesions. B. S. Brody, New Haven.—p. 337.

Endocrinology, Los Angeles

26:941-1130 (June) 1940. **Partial Index**

Adrenal Cortical Virilism. F. D. W. Lukens and H. D. Palmer, Philadelphia.—p. 941.
Estrogenic Effects on Tubal Contractility and Vaginal Secretion in the Menopause: Study of Twenty-Four Cases with Aid of Uterotubal Insufflation. P. Bernstein and M. Feresten, New York.—p. 946.
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Relationship Between Secretory Cells of Pars Nervosa of Hypophysis and Classic Neuroglia. M. Griffiths.—p. 1032.
Effects of Ovariectomy and Administration of Progesterone on Adrenal X Zone and Uterus. Evelyn Howard and S. Gengradom, Baltimore.——p. 1048.
Effect of Testosterone, Estrone and Estradiol Applied Locally to Penis of Rat. H. S. Wigodsky and R. R. Greene, Chicago.—p. 1078.
Effects of Testosterone Propionate on Pregnancy and on Passage of Ova Through Oviducts of Mice. H. O. Burdick, B. B. Emerson and R. Whitney, Alfred, N. Y.—p. 1081.
Urolithiasis in Rat After Injection of Testosterone Propionate. J. Gershon-Cohen, H. Shay, K. E. Paschkis and S. S. Fels, Philadelphia.—p. 1087.

Illinois Medical Journal, Chicago

77:549-636 (June) 1940

Relation of the Illinois State Medical Society to 100 Years of Progress. J. H. Hutton, Chicago.—p. 565.
The Illinois State Program for Crippled Children. P. H. Harmon, Springfield.—p. 579.
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A Century of Medical Progress. M. Fishbein, Chicago.—p. 604.
Epitomized Record of Progress of Medicine During the Last Hundred Years 1840-1940. C. J. Whalen, Chicago.—p. 612.

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66:335-420 (June) 1940

Cardiac Arrhythmia During Cheyne-Stokes Respiration. E. Matthews and W. B. Wood Jr., Baltimore.—p. 335.
Hypertrophia Musculorum Vera (Dystrophia Musculorum Hyperplastica) Associated with Hypothyroidism: Case Study. F. H. Hesser, Baltimore.—p. 353.
Factors Influencing Plasma Prothrombin in Newborn Infant: III. Study of Vitamin K Activity of Various Naphthohydroquinone Derivatives. L. M. Hellman, W. T. Moore and L. B. Shettles, Baltimore.—p. 379.
The Patient as a Person. G. C. Robinson, Baltimore.—p. 390.
Native Hormones of Posterior Pituitary Gland: Pressor and Oxytocic Principles. M. Rosenfeld, Baltimore.—p. 398.

Journal of Experimental Medicine, New York

71:731-880 (June) 1940

Utilization of Iron and Rapidity of Hemoglobin Formation in Anemia Due to Blood Loss. P. F. Hahn, J. F. Ross, W. F. Bale and G. H. Whipple, Rochester, N. Y.—p. 731.
Constituents of Elementary Bodies of Vaccinia: I. Certain Basic Analyses and Observations on Lipid Components of Virus. C. L. Hoagland, J. E. Smadel and T. M. Rivers, New York.—p. 737.
I. Poliomyelitic Virus in Human Stools. J. D. Trask, J. R. Paul and A. J. Vignec, New Haven, Conn.—p. 751.
II. Poliomyelitic Virus in Urban Sewage. J. R. Paul, J. D. Trask and S. Gard, New Haven, Conn.—p. 765.
III. Method for Detecting Poliomyelitic Virus in Sewage and Stools. S. Gard, New Haven, Conn.—p. 779.
Activating, Transforming and Carcinogenic Effects of Rabbit Papilloma Virus (Shope) on Implanted Tar Tumors. P. Rous and J. G. Kidd, New York.—p. 787.
Transplantable Rabbit Carcinoma Originating in Virus-Induced Papilloma and Containing Virus in Masked or Altered Form. J. G. Kidd and P. Rous, New York.—p. 813.
Dwarf Mutation in Rabbit: Constitutional Influence on Homozygous and Heterozygous Individuals. H. S. N. Greene, Princeton, N. J.—p. 839.
Action of Renin on Rabbits with Renal Hypertension. J. Taggart and D. R. Drury, Los Angeles.—p. 857.

Journal of Lab. and Clinical Medicine, St. Louis

25:897-1012 (June) 1940. **Partial Index**

Role of Coenzymes I and II in Blood of Persons with Pneumococcic Pneumonia. R. W. Vilter, W. B. Bean, J. M. Ruegsegger and T. D. Spies, Cincinnati.—p. 897.
Water Content of Myocardium in Hypertrophy and Chronic Congestive Failure. H. Gross, New York.—p. 899.
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Lipid, Carbohydrate and Moisture Content of Liver in Diabetes Mellitus. Nellie Halliday, Boston.—p. 926.
Relationship Between Plasma Proteins and Erythrocyte Sedimentation Rates in Chronic Atrophic Arthritis. R. Davison, Tucson, Ariz., with technical assistance of Mildred Woolley and Eleanor Donovan.—p. 935.
Significance of Urinary Chlorides in Cases of Pneumonia Treated with Sulfapyridine, with Some Remarks on Secondary Temperature Rise. W. Antopol and J. Churg, Newark, N. J.—p. 946.
*Chickenpox Following Contact with Herpes Zoster: Report of Two Minor Epidemics. M. L. Blatt, Mary Zeldes and A. F. Stein, Chicago.—p. 951.
Problem of Diarrheas of Childhood: Study of 543 Attacks in Children at Beirut, Syria. J. L. Moore and E. W. Dennis, Beirut, Syria.—p. 955.
Quantitative Study of Syphilitic Serum. R. A. Greene, E. L. Breazeale and C. C. Croft, Tucson, Ariz.—p. 972.
Study of Demonstration of Tubercle Bacilli in Urine by Means of Phosphate Flocculation. J. H. Hanks and H. A. Feldman, Washington, D. C.—p. 974.

Chickenpox Following Contact with Herpes Zoster.—Blatt and his associates describe a clinical syndrome resembling chickenpox that several patients experienced after contact with herpes zoster. The original source of the virus in one epidemic apparently was a bedridden child in the tuberculosis ward. His only contact was with nurses, attendants, medical personnel and other patients in his own six bed room. No visitors were allowed. None of his contacts were known to have had chickenpox or herpes zoster. Eleven weeks after his admission to the ward, two patches of vesicles developed. There were no constitutional symptoms. A diagnosis of herpes zoster was made and confirmed by the divisions of dermatology and contagious diseases. Thirteen days after the eruption of herpes, vesicles developed on a second child who had been in this room for one year prior to the admission of the child with herpes. This second child had had no exposure other than with the personnel in attendance. On advice of a consulting physician from the contagious division, this child was transferred with the diagnosis of chickenpox. Twelve days later the last crust had disappeared and the child was transferred back to the tuberculosis ward. A secondary case of chickenpox occurred in a child admitted to an adjacent room five days prior to the onset of chickenpox in the second child. This third child had not had chickenpox previously, nor had she had any recent contact with contagious diseases. As in the other rooms in this ward, no visitors were allowed. Twenty-one days after her entrance to the hospital a universally disseminated eruption that passed through the papular, vesicular and later the crusting stages developed. She was transferred to the contagious division as having chickenpox. There were no further cases. In a second epidemic, which occurred in a medical ward, the source of the virus could be traced to a nurse who had herpes zoster. An eruption developed in this nurse who had had chickenpox in childhood. The lesions were pinhead-sized vesicles on an elevated erythematous base. A week after their onset she was referred to a dermatologic consultant, who made a diagnosis of herpes zoster. Chickenpox-like lesions developed within eighteen and fourteen days, respectively, in two children exposed to this nurse. These children were not allowed to have visitors. The diagnosis was confirmed by a consultant from the contagious division, to which the children were immediately transferred. The authors state that it is striking that in each episode, in spite of the large number of children in contact with herpes zoster and the resulting secondary eruptions, only four cases designated as chickenpox occurred. In contrast to herpes zoster and the resulting secondary eruptions, chickenpox epidemics are usually widespread. In these cases, as in chickenpox, the varicelliform eruption appeared from thirteen to twenty-one days after exposure to herpes zoster. This and the fact that three of the patients were in the hospital for more than a month with no visitors would indicate that the relationship between herpes zoster and chickenpox is more than a mere coincidence. A review of the literature still leaves doubt as to whether or not the virus of the two diseases is identical.

Journal of Neurophysiology, Springfield, Ill.

3:283-370 (July) 1940

Hypothalamic Lesions and Pneumonia in Cats: Notes on Behavior Changes. E. W. Haertig and J. H. Masserman, Chicago.—p. 293.
Progression Movements Elicited by Subthalamic Stimulation. W. H. Waller, Vermillion, S. D.—p. 300.
Electrical Activity of Lateral Geniculate of Cats Following Optic Nerve Stimuli. G. H. Bishop and J. S. O'Leary, with assistance of C. B. Mueller, St. Louis.—p. 308.
Integration of Locomotor Behavior Patterns of Hagfish. B. Campbell, Oklahoma City.—p. 323.
Effects of Heating Hypothalamus of Dogs by Diathermy. A. Hemingway, T. Rasmussen, H. Wikoff and A. T. Rasmussen, Rochester, Minn.—p. 329.
Role of Neocortex in Regulating Postural Reactions of Opossum (Didelphys Virginiana). R. B. Bromiley and C. M. Brooks, Baltimore.—p. 339.
Chemical Constitution and Anesthetic Potency in Relation to Cortical Potentials. H. K. Beecher, Boston.—p. 347.
Ocular Movements from Occipital Lobe in Monkey. A. E. Walker and T. A. Weaver Jr., Chicago.—p. 353.
Nature of First Visible Contractions of Forelimb Musculature in Rat Fetuses. W. L. Straus Jr. and G. Weddell.—p. 358.

Journal of Thoracic Surgery, St. Louis

9:471-582 (June) 1940

*Large Infected Solitary Pulmonary Cysts Simulating Empyema. H. C. Maier, New York, and C. Haight, Ann Arbor, Mich.—p. 471.
Joint Manifestations Associated with Intrathoracic Tumors. W. Van Hazel, Chicago.—p. 495.
Role of Pleural Lymphatics in Pathogenesis of Cold Abscesses of Chest Wall and Paravertebral Abscesses. H. E. Burke, Ray Brook, N. Y.—p. 506.
*Comparative Report on Infection of Thoracoplasty Wounds: Experiences with Ultraviolet Irradiation of Operating Room Air. R. H. Overholt and R. H. Betts, Boston.—p. 520.
Chronic Inflammatory Lesions of Lung Simulating Bronchiogenic Carcinoma. S. O. Freedlander and S. E. Wolpaw, Cleveland.—p. 530.
Control of Hemorrhage in Intrapleural Pneumolysis: Indication for This Operation in Tropics. O. Paneth, Kaban Djahe, Sumatra.—p. 544.
Effective Method for Closure of Cannula Openings Following Internal Pneumolysis. C. D. Whelchel and E. W. Grove, Alto, Ga.—p. 549.
Clinical Measurement of Pulmonary Elasticity: Comparison of Methods of Christie and McIntosh and of Neergaard and Wirz. J. R. Paine, Minneapolis.—p. 550.
Thoracic Lipomas. R. G. McCorkle, C. J. Koerth and J. M. Donaldson Jr., San Antonio, Texas.—p. 568.

Pulmonary Cysts Simulating Empyema.—Maier and Haight discuss three cases of large solitary intrapulmonary cysts lined with stratified columnar epithelium and containing purulent material. At the time the patients came under observation the condition simulated and was diagnosed as empyema. Two of the three cases were treated for empyema for some time before the correct diagnosis was realized. Drainage alone will not

produce obliteration of epithelized cysts. An epithelized pulmonary cyst fails to diminish in size despite adequate drainage over long periods. Following removal of the epithelized cyst wall, obliteration of the space readily occurs. Healing is accomplished for the most part by granulation, with elevation of the diaphragm, retraction of the thoracic wall and shifting of the mediastinum, and to some extent by the expansion of the adjacent pulmonary tissue. The importance of each of these factors varies in different cases. In each of the cases reported, the cyst had been drained for more than two years before it was removed. Two years after the operative procedures the patients are well and have healed thoracic wounds. Treatment of large infected pulmonary cysts with an epithelial lining should consist first in surgical drainage of the purulent contents by thoracotomy. In cases of suspected cyst, a rib resection rather than an intercostal type of drainage should be done to enable the operator to visualize the interior of the cavity and to secure a biopsy. If the first biopsy specimen is inconclusive, another specimen should be obtained. The most certain method of treating the epithelized pulmonary cyst is removal of the lobe containing the cyst or by enucleation of the cyst itself. With the infected contents of the cyst drained, the inflammatory reaction should subside and the patient's general condition should be good before operations are carried out. The patients are usually children or young adults and bear the procedures well.

Infection of Thoracoplasty Wounds.—Overholt and Betts base their report on 701 consecutive thoracoplasties performed in the course of two and one half years. There was a reduction in the incidence of serious wound complications to 0.49 per cent in clean cases. They attribute this to a change in the technic of wound closure and to ultraviolet irradiation of the operating room air. They observed that when an infection did occur it was likely to be present around a consecutive series of sutures. The use of a continuous suture in the skin was then discarded, and individual milliners' needles for separate sutures threaded with fine silk were substituted. Silver foil was used to cover the suture line. Following the institution of this method of closure, seventeen infections occurred in 261 wounds, or in 6.53 per cent, as against approximately 15 per cent reported in the literature. Of 287 thoracoplasties performed under ultraviolet irradiation in one hospital five became infected; three were superficial and two were deep. In a second hospital similarly equipped, 124 operations were carried out and six wounds became superficial.y infected. The extent of the infection was limited in all cases to one or two skin sutures. Thus in a total of 411 operations there were eleven infections (2.67 per cent) but only two, or 0.49 per cent, were deep and of clinical significance.

Kansas Medical Society Journal, Topeka

41:233-276 (June) 1940

*Treatment of Acute and Chronic Brucellosis. F. E. Angle and W. H. Algie, Kansas City.—p. 233.
Treatment of the Commoner Injuries of the Hand. L. S. Nelson, Salina.—p. 236.
Aleukemic Myelosis in Remission Simulating Banti's Disease. D. H. Miller and A. H. Pemberton, Wichita.—p. 240.
Vitamin K. L. Lewis, McPherson.—p. 243.
Nonradiating Low Back Pain. R. J. Dittrich, Fort Scott.—p. 247.
Epidemic Cerebrospinal Meningitis: Comparison of Serum and Sulfanilamide Treatment. R. M. Isenberger, Kansas City.—p. 250.
Retroperitoneal Cyst Simulating Appendicitis. M. A. Walker, C. E. Coburn and Alice Pendleton, Kansas City.—p. 251.

Treatment of Brucellosis.—Angle and Algie state that the acute form of undulant fever is a self-limiting disease. Treatment will often produce the apparent cure of a patient who is undoubtedly recovering because of his own resistance. They believe that the majority of cases of acute undulant fever have gone unrecognized and untreated to complete recovery. The various dye substances, including among others acriflavine, gentian violet, mercurochrome and metaphen, have proved of little or no value. Neoarsphenamine has not proved to be of value. Fuadin, the English advocated method, has not stood the test of time. Foshay's serum, which is not available commercially, has been tried extensively by him. He is of the opinion that it is a specific therapy up to approximately eight months. After this, for some reason which he is unable to explain, the serum is of no value. Nucleoprotein extract of Brucella has been used and reported favorably. Here again the preparation is not available commercially and thus has not had a general trial. One of the "shock" methods of therapy perhaps represents the best method now available. The evidence points to specific vaccine as the preferred method. Before treating a case of chronic brucellosis, any possible foci of infection should be eradicated. Sulfanilamide is not a specific for brucella infection. As a large number of persons present serologic evidence of infection as a part of an immune reaction, care should be taken before a diagnosis of acute or chronic brucellosis is made. As recurrence may come after years of apparent cure, care should be used in interpreting any method of therapy. If specific vaccine is used, it should be administered intramuscularly or in selected cases intravenously in small doses. Not more than from three to five injections should be given. Adequate time should be allowed for interpretation of the result because in individuals sensitive to this antigen fever can be produced at any time even after complete symptomatic recovery. A complete blood count is of aid in both the diagnosis and the prognosis of brucella infection. A definite leukopenia and lymphocytosis are almost always present in active acute or chronic disease. When the blood count is elevated and there is an increase in the polymorphonuclear leukocytes the authors always question the diagnosis. A high caloric diet is important in the management of patients with prolonged fever. The patient showing a blood picture of secondary anemia is given an adequate amount of iron. As the patient recovers from brucellosis there is a definite disappearance of his subjective symptoms, increase in weight and gradual disappearance of fever, the agglutination titer of the blood diminishes, the blood picture returns to normal and the neurologic symptoms subside.

Medical Annals of District of Columbia, Washington

9:189-226 (June) 1940

Progress and Personalities in Early French Surgery. J. H. Lyons, Washington.—p. 189.
Newer and Safer Technic in Management of Appendicitis with Perforation. E. A. Cafritz, Washington.—p. 197.
Perforated Peptic Ulcer: Suggested Method of Treatment. O. C. Cox, Washington.—p. 202.
Healing of Intracapsular Fractures of Neck of Femur. J. F. Elward, Washington, and N. Rudner, New York.—p. 205.
Third Annual Report of the Diabetic Camp for Children. K. H. Mish, S. Benjamin, B. Manchester, E. C. Rice and Leila Hulbert, Washington.—p. 212.

New England Journal of Medicine, Boston

222:985-1028 (June 13) 1940

*Agnogenic Myeloid Metaplasia of Spleen: Syndrome Simulating Other More Definite Hematologic Disorders. H. Jackson Jr., F. Parker Jr. and H. M. Lemon, Boston.—p. 985.
Pentothal Sodium Anesthesia for Encephalography. M. J. Nicholson and L. F. Sise, Boston.—p. 994.
Nurses and Doctors. S. Rushmore, Boston.—p. 997.
Hematology. W. Dameshek, Boston.—p. 1000.

Agnogenic Myeloid Metaplasia of Spleen.—Jackson and his associates point out that a varying degree of extramedullary myelopoiesis occurs in a wide variety of pathologic conditions. It has been seen in carcinoma metastases to bone, it is not infrequent in certain infectious states such as scarlet fever, and it has been noted in generalized sepsis, tuberculosis of the spleen and areas of pathologic calcification and ossification. Under such circumstances usually the primary underlying disease is patently manifest and the ectopic blood formation is minimal in amount. In myelogenous leukemia the extramedullary myelopoiesis reaches its greatest height. Here again, however, the process is of secondary importance. The authors draw attention to another class of patients with myeloid metaplasia in whom this abnormal process assumes major proportions and in whom it may therefore be responsible for serious errors in diagnosis. They designate this type of myeloid metaplasia of the spleen as "agnogenic"; that is, of unknown etiology. In a total of ten cases the spleen showed marked myeloid metaplasia, scattered foci of immature red and white blood cells and megakaryocytes throughout a slightly or markedly fibrosed organ. In cases which came to necropsy similar foci of ectopic blood formation in the liver and lymph nodes were occasionally found. There was not the uniform distribution of immature cells seen in the organs of leukemic patients, and immature cells of the red cell

series were present in greater numbers than in that disease. The malpighian corpuscles were for the most part uninvolved. The bone marrow was variously fibrotic, hyperplastic, aplastic or normal. In no instance was it even suggestive of leukemia. In three cases the diagnosis of myeloid metaplasia seemed clearly established and only symptomatic treatment was given. All three patients are alive. In one a diagnosis of hemolytic jaundice was made and splenectomy was performed. The patient died three days after operation. In two cases no definite diagnosis was made, but splenectomy was advised and carried out. In neither case was there any improvement in the peripheral blood picture and both patients died within a year. In four cases a definite diagnosis of myelogenous leukemia was made. One patient was treated symptomatically and died three years from onset. The three others were given roentgen treatment. Two died within six weeks; in the third case no real benefit occurred and the patient succumbed to bronchopneumonia two years later. The average duration from onset to date of death was 10.8 years. In four cases the symptoms dated back over fifteen years. The chief symptoms were weakness, abdominal distress and a hemorrhagic tendency. The principal conditions found were a progressive enlargement of the spleen, a moderately elevated or slightly depressed white cell count and the constant presence of immature red and white cells in a peripheral blood. In view of the apparent uselessness and possible harm arising from irradiation or splenectomy, it is of the greatest importance to recognize this condition and to undertake only symptomatic and supportive treatment when it has been proved to be present.

South Carolina Medical Assn. Journal, Greenville

36:159-184 (June) 1940

Congenital Ganglioneuroma of Nose: Report of Case. M. Crook, Spartanburg.—p. 159.
Physiopathologic Consideration of Bright's Disease. M. W. Beach, Charleston.—p. 160.

Surgery, St. Louis

7:809-988 (June) 1940

Changes in Pressure in Antecubital and Saphenous Veins During Abdominal Operations. J. R. Veal and H. H. Hussey, Washington, D. C.—p. 809.
Meteorologic Factor in Pulmonary Embolism. G. de Takats, A. Mayne and W. F. Petersen, Chicago.—p. 819.
*Further Report on Treatment of Undescended Testes by Hormone Therapy at the University of Minnesota Hospitals: Discussion of Spontaneous Descent of Testis and Evaluation of Endocrine Therapy in Cryptorchidism. C. E. Rea, Minneapolis.—p. 828.
*Late Results of Injection Treatment of Hernia. L. Dobson, San Francisco.—p. 836.
Traumatic Hemothorax: Analysis of 276 Cases. F. L. Cato and W. D. Norman, New Orleans.—p. 848.
Adamantinoma of Tibia. R. Hebbel, Minneapolis.—p. 860.
Increased Collateral Blood Supply to Kidney in Renal Hypertension. S. Goldberg, S. Rodbard and L. N. Katz, Chicago.—p. 869.
Transplantation of Lower Scapula Within Thoracic Cage Following Upper Thoracoplasties. L. J. Leahy, Buffalo.—p. 875.
Chronic Undermining Ulcer of Skin Due to Beta Hemolytic Streptococcus. H. H. Johnson and H. P. Royster, Cleveland.—p. 883.
Tumors of Male Breast. H. Charache, Brooklyn.—p. 889.
Appendiclausis: Appendical Obstruction Simulating Acute Appendicitis. L. S. Cherney, San Francisco.—p. 900.
Simplified Plastic Operation for Hump, Hook and Twist of Nose. J. Sarnoff, Brooklyn.—p. 908.
Spinal Anesthesia in Arabia. P. Harrison, Kalamazoo, Mich.—p. 910.
Bronchoscopic Experiences with Lung Tumors. E. N. Broyles and G. E. Fisher, Baltimore.—p. 918.

Undescended Testes and Endocrine Therapy.—Of the thirty-two patients with thirty-six undescended testes that Rea treated with anterior pituitary-like substance, descent occurred in six patients and in seven ectopic testes (one bilateral case). There was no uniformity in the dosage or length of treatment in the successful cases. The gonads in these cases were retained inguinally in five and abdominally in two. Of the twenty-six patients in whom descent did not follow endocrine therapy, the position of the gonad was inguinal in eighteen and abdominal in eight. All the patients received at least 3,750 units of anterior pituitary-like substance during the course of treatment. The author believes that one reason for the successful results in some reported series is undoubtedly the inclusion of pseudocryptorchidism. A final estimate of the value of gonadotropic substance in the treatment of ectopic testes is impossible, as the incidence of spontaneous descent is not accurately known. Treatment should be deferred until the child is from 9 to 11 years of age, since the testis does not grow grossly or microscopically until then (Wangensteen) and spontaneous descent is possible. Endocrine therapy should be tried first and, if no results are obtained, an orchiopexy should be performed. On the basis of his experience the author states that spontaneous descent or descent following the use of gonadotropic substance in cases of true undescended testis is a rare occurrence.

Late Results of Injection Treatment of Hernia.—From September 1935 to June 1938 Dobson treated seventy-four patients, seventy males and four females, with 101 hernias by the injection method. There were sixty-eight indirect inguinal hernias, twenty-one direct inguinal hernias, ten postoperative inguinal hernias, one postoperative femoral and one umbilical. Only patients who had had their trusses off for more than six months after the last injection are included in the study. Follow-up studies up to two and one half years were obtained on fifty-three indirect and nineteen direct inguinal hernias, six of the postoperative ones, the one postoperative femoral and the one umbilical hernia. There were 37.73 per cent recurrences among the indirect inguinal hernias; 68.42 per cent of the direct inguinal hernias and all of the postoperative inguinal hernias recurred. All of the postoperative recurrent inguinal hernias followed had direct defects. Six months after beginning the injection treatment the results were most promising and it seemed that all types and sizes of hernias were being cured. Most of the direct inguinal hernias recurred within three to four months after the last injection. All the cases showed signs of disappearance of the scar tissue within two to three months following the last injection. Since the sac is rarely obliterated, the whole basis of cure in the injection treatment of hernia is the fibrous tissue which persists between the fascial planes, muscle layers and spermatic cord. These adhesions hold the hernial sac compressed and prevent omentum or intestine from entering the neck of the sac. The injection treatment should be used only in small indirect inguinal hernias in patients with otherwise good abdominal structures who will not or cannot be operated on.

Tennessee State Medical Assn. Journal, Nashville

33:197-242 (June) 1940

The Small Town Clinic Hospital—Its Place in the Community. W. G. Rhea, Paris.—p. 197.
Some Clinical Manifestations Resulting from Endamoeba Histolytica Infections. E. L. Turner and W. A. Beck, Nashville.—p. 203.
Medical Aspects of Menopause. L. E. Burch, Nashville.—p. 208.
Drugs in Treatment of Heart Disease. J. L. Bibb, Chattanooga.—p. 213.
Prothrombin Deficiency and Vitamin K in Newborn Period. W. H. Thompson, Minneapolis.—p. 218.
Sulfanilamide as Prophylaxis in Scarlet Fever. C. B. Laughlin, Greeneville.—p. 223.

Virginia Medical Monthly, Richmond

67:327-392 (June) 1940

Use of Protamine Zinc Insulin in Treatment of Diabetes Mellitus. H. B. Mulholland, University.—p. 327.
Early Myocardial Insufficiency. W. P. Adams, Norfolk.—p. 337.
The Care of the Sick Child. E. L. Kendig Jr., Victoria.—p. 342.
Incidence and Significance of Shock in Patients with Acute Head Injuries, with Special Reference to Prevention of Post-Traumatic Infections. J. M. Meredith, University.—p. 345.
The Rheumatic Problem. J. R. Hamilton, Nassawadox.—p. 357.
Endocrinology Briefs: Parathyroid Glands. J. P. Lynch, Richmond.—p. 360.
Medical Aspects of Primary Neoplasm of Lung: Analysis of Thirty Cases. W. H. Higgins, Richmond.—p. 362.
*Herpes Simplex of Lips: New Method of Treating the Solitary Vesicle. W. M. Brunet, Chicago.—p. 367.
Paralytic Ileus and Intestinal Obstruction Simulated by Disease of Urinary Tract. S. D. Failla, Durham, N. C., and E. M. Chapman, Chelsea, Mass.—p. 368.
Unusual Gunshot Wounds: Case Reports. B. A. Hopkins, Stuart.—p. 372.
Prostigmine in Induction of Labor. S. Robins, Richmond.—p. 374.
The Healing Process in Fractures. M. H. Todd, Norfolk.—p. 376.

Herpes Simplex of Lips.—Brunet points out that many of the large single vesicles of herpes simplex which occur on the lips, if carefully inspected with a magnifying glass, will be found to have the pattern of a small wheel. The number of segments varies. The treatment that he has used on a number of patients and on himself consists of multiple punctures with a sterile fine hypodermic needle. When this is done tension is immediately released, the itching and burning are relieved and a scab forms quickly and the lesion usually heals within a week.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Ophthalmology, London

24:265-316 (June) 1940

Ophthalmic Injuries in War. N. I. Shimkin.—p. 265.
Luxatio Bulbi: Case. E. C. Zorab and W. L. Burns.—p. 286.
Cyclodiathermypuncture in Cases of Glaucoma. A. Vogt.—p. 288.
Amblyopia Ex Anopsia in Children. J. H. Young.—p. 297.

British Journal of Radiology, London

13:185-220 (June) 1940

Maternal Mortality and Radiology. L. A. Rowden.—p. 185.
Emission and Transmission of X and Gamma Radiation. G. W. C. Kaye and W. Binks.—p. 193.
Fluorine Osteosclerosis: Two Cases. J. Wilkie.—p. 213.
Frontal Cephalhematoma. A. Schüller.—p. 218.

British Journal of Urology, London

12:75-160 (June) 1940

Complicated Injuries of Urinary Tract. G. Gordon-Taylor.—p. 75.
Surgical Treatment of Diverticula of Bladder. G. de Illyés.—p. 104.
Seasonal Variation in Death Rate of Suprapubic Prostatectomy. F. J. F. Barrington.—p. 121.

British Medical Journal, London

1:919-960 (June 8) 1940

Circulation in Relation to Shock. J. S. McDowall.—p. 919.
Notes on Rubella, with Special Reference to Certain Rheumatic Sequelae. R. A. Bennett and W. S. C. Copeman.—p. 924.
Basal Metabolism Test in Thyrotoxicosis: Its Value to the Clinician. L. Martin.—p. 927.
Convulsions After Vinethene Anesthesia. F. K. Boston.—p. 929.
Agranulocytosis Following Chemotherapy with Small Dosage. A. W. Spain.—p. 930.

1:961-1004 (June 15) 1940

Sulfonamide Treatment of Gonorrhea: Results of Treatment. R. C. L. Batchelor, R. Lees and G. M. Thomson.—p. 961.
Late Relapse Following Treatment of Gonorrhea with Sulfapyridine. S. M. Laird.—p. 967.
*Treatment of Spasmodic Torticollis by Psychotherapy. W. H. Whiles.—p. 969.
Multiple Emboli Treated Surgically. J. A. MacFarlane.—p. 971.
Cyanosis and Anoxemia in Gas and Oxygen Anesthesia. R. L. Wynne.—p. 972.
Ehlers-Danlos Disease: Case. J. E. Murray and M. E. Tyars.—p. 974.

Treatment of Spasmodic Torticollis by Psychotherapy.—Whiles treated four cases of spasmodic torticollis by psychotherapy. The spasm was of the spinal accessory distribution type and there were no other neurologic signs and no history of rheumatism. The spasm assumed a compulsive character and was of long duration. The first patient, an unmarried woman of 37, secured complete relief through superficial analysis associated with suggestion and relaxation. She returned to work and became more mature in her outlook, more cooperative and independent. Her symptom symbolized her previous attitude of turning away from sex, life and responsibility. The second patient, a married woman of 41, secured complete freedom from symptoms through suggestion and relaxation and she was able to take up her former interests and make social contacts. Her symptom represented her desire to turn away from people because of the repressed guilt for her father's death from heart disease. Full analysis of the third patient, a married woman of 44, was impossible owing to irregular attendance and lack of cooperation. Relaxation and suggestion brought slight relief, but the symptoms were still present when the patient discharged herself. The psychologic background and the symbolic nature of her symptoms were evident. The last patient, a married woman of 26, was completely free from symptoms after analysis. She was able to go out alone, was free from embarrassment in company and her sexual life became normal. Her symptom symbolized her attitude of turning away from her sexual role as a woman. The more carefully the cases are studied, the more evident it becomes that the symptom is not an isolated factor but the response of an inadequately adjusted personality to a period of particular stress. Efforts to correct the condition must not be directed to the torticollis alone or simply to a disclosure of its genesis, but to a fundamental attempt to readjust the personality to life.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

47:109-236 (April) 1940

*Leukorrhea in Pregnancy: Study of 200 Cases. W. G. Liston and L. G. Cruickshank.—p. 109.
Bony Pelvis and Its Influence on Labor: Radiologic and Clinical Study of 500 Women. J. G. H. Ince and M. Young.—p. 130.
Hydatid (Echinococcal) Cysts of Female Pelvis. B. Evans.—p. 191.
Granulosa Cell Tumor with Precocious Sexual Development in Child Aged 6. F. Stabler and J. G. Thomson.—p. 199.
Simultaneous Intra-Uterine and Extra-Uterine Pregnancy. S. Mitra.—p. 206.
Osteomyelitis of Pubic Bones and Staphylococcic Septicemia Complicating Pregnancy: Unusual Changes in Presentation of Fetus During Later Weeks of Pregnancy. G. Rowarth.—p. 213.

Leukorrhea in Pregnancy.—Liston and Cruickshank found the vaginal discharge to be normal in only forty of 200 pregnant women supposed to be suffering from leukorrhea. By normal the authors mean that pus cells were less numerous than epithelial cells, the bacterial flora consisted wholly of Döderlein's bacilli, the p_H of the vaginal contents lay between 4 and 5, and glycogen was abundant in the epithelial cells. Cervical lesions, including erosions, were present in seventy-nine of the 200 cases. More than half of these cases were complicated by other causes of leukorrhea. The condition of the cervix of thirty-one women was the possible explanation of the leukorrhea. The more severe forms of cervical lesions were associated with abnormal features of the vaginal contents, for pus cells became more numerous, the bacterial flora tended to drift toward types 2 and 3, the hydrogen ion value was less acid, and glycogen was less abundant in the epithelial cells. There were only four cases of gonorrhea. The parasite of vaginal thrush was the cause of the leukorrhea in forty-nine. This infection is easily overlooked unless films are made from the white patches characteristic of the disease. The diagnosis should be made by finding the hyphal filaments of the fungus. The blastospores of this fungus may be confused with yeast cells. Trichomonas vaginalis was responsible for the leukorrhea of seventy-five of the 200 women. In all these cases pus cells predominated over epithelial cells in the vaginal films, and the majority of the cases presented a bacterial flora of type 3. The p_H of the vaginal contents lay generally between 5 and 6. Recovery was associated with a return of the p_H to between 4 and 5, and this was associated with a change in the type of the bacterial flora from type 3 to 1 through type 2. Glycogen was generally deficient in the epithelial cells. The condition was in some cases complicated by cervicitis, thrush or gonorrhea. Eight of the 200 cases could not be classified. Some of these patients showed a thin, watery discharge with numerous epithelial cells, comparatively few pus cells, large numbers of organisms of type 3 and p_H about 6. No cause for this type of leukorrhea was apparent. A further study of leukorrhea on similar lines seems desirable in order to elucidate the fundamental causes of this common but much neglected condition.

Lancet, London

1:1071-1110 (June 15) 1940

Pulmonary Tuberculosis: Diagnosis and Some Aspects of Treatment. F. G. Chandler.—p. 1071.
*Serum Phosphatase in Cases of Bone Tumor. S. Cade, N. F. Maclagan and R. F. Townsend.—p. 1074.
Leukopenia and Mucosal Lesions Following Sulfapyridine Therapy. Helen M. Mayo and Constance Finlayson.—p. 1075.
Erythroblastemia and Its Value in Diagnosis of Neoplastic Infiltration of Bone Marrow. F. P. Weber.—p. 1077.
Decurvon: Pectin-Insulin with Protracted Action. B. Brahn.—p. 1078.
*Nutritional Deficiency of Vitamin K in Man. H. Scarborough.—p. 1080.
Infective Mononucleosis and the Paul-Bunnell Test. H. P. Himsworth.—p. 1082.
Cinebronchography (Cinematography Through the Bronchoscope). J. E. G. McGibbon.—p. 1083.
Vi Agglutination in Detection of Typhoid Carriers. E. S. Horgan and A. Drysdale.—p. 1084.

Serum Phosphatase in Cases of Bone Tumor.—Cade and his associates performed serial estimations of serum phosphatase by the method of King and Armstrong in twenty-eight cases of bone tumor. The normal range for this method is from 3 to 13 units. Most of the patients were undergoing treatment by radium bomb or by x-rays. Raised values were found in eleven out of twelve cases of osteogenic sarcoma, in three out of five cases of osteoclastoma and in six out of eight cases with bone metastases, and all of the three cases of Ewing's

tumor showed values near the upper normal limit. Radiotherapy in a case of osteogenic sarcoma produced a fall in serum phosphatase, but normal limits were not regained, suggesting either that the malignant osteoblasts had not all been destroyed or that metastases had developed. After amputation of the leg for a radium burn, the serum phosphatase remained high and an x-ray examination of the chest revealed metastases of which there was no clinical evidence. In another case normal values were regained for a time, but then a rise took place which was associated with further extension of the tumor. In a case of osteoclastoma the initial normal values rose above normal during the treatment. The authors interpret this as indicating repair by normal osteoblasts after the osteoclastic tumor cells had been destroyed. Seventeen cases of carcinoma of the breast and two cases of prostatic carcinoma were investigated. The readings were normal in mammary carcinoma but above normal in the prostate cases. On the strength of the high reading (89 units) in one case of prostatic carcinoma, a roentgenogram was taken which revealed multiple metastases. The results as a whole appear to fit in well with the hypothesis that the increased amount of serum phosphatase in cases of bone tumor reflects the level of osteoblastic activity. The authors answer the question of whether the estimations of serum phosphatase are of clinical value as follows: 1. In osteogenic sarcoma the test is of value in following the course of treatment and in detecting the onset of metastases. 2. In osteoclastoma and in Ewing's tumor the estimation merely reflects the attempts at repair which are known to be present and is not of any particular value. 3. In secondary deposits in bone it is obviously useful to be able to detect clinically latent metastases. In prostatic carcinoma the estimation of serum phosphatase appears to be a useful routine test, which might well be done before any radical operation is attempted.

Nutritional Deficiency of Vitamin K in Man.—Scarborough reports the results of investigations into the levels of plasma prothrombin in clinical hypovitaminoses. He calls attention to an important point in the technic of the determination of the prothrombin time. All the eighteen cases investigated presented clear clinical evidence of deficiency of one or more vitamins. Further evidence in support of the diagnosis of such a deficiency was obtained by a study of the previous diets of the patients and by laboratory tests. None of the patients were jaundiced and none showed clinical evidence of hepatic disease. Vitamin A deficiency was demonstrated by a dark adaptation method. Vitamin B_1 deficiency was determined by estimation of the vitamin in the blood by a modification of the Schopfer-Meiklejohn method. Vitamin C deficiency was determined by an ascorbic acid saturation test. Vitamin P deficiency was determined by measurement of the capillary resistance. Vitamin K deficiency was assessed in terms of the prothrombin time determined according to the original method of Quick et al. The answer to the question of whether a spontaneous deficiency of vitamin K, as determined by a decreased plasma-prothrombin level, may arise in man in the absence of jaundice and as the result of a dietary deficiency of vitamin K appears to depend on the method used for determining the prothrombin time. If the plasma prothrombin is determined by the method in general use (Quick et al.), the answer is "no." If the deficiency is assessed by the dilution method described by Kark and Lozner, the answer is "yes." In view of the large and steadily increasing amount of work on vitamin K it is important that the methods of determining plasma prothrombin be reconsidered. Since there was a deficiency of several vitamins in all twenty-two cases investigated, it is probable that the method of Kark and Lozner is superior to that in general use.

South African Medical Journal, Cape Town

14:167-186 (May 11) 1940

*Active Tetanus Immunization and Combined Tetanus-Typhoid Immunization with Tetanus Anatoxin and Typhoid Endotoxoid Vaccine. E. Grasset and A. I. Girdwood.—p. 169.

Combined Tetanus-Typhoid Immunization.—According to Grasset and Girdwood, active tetanus immunization has been introduced in the British army since the end of 1938. The first application of active tetanus immunization to man, in 1926, by Ramon and Zoeller, showed that a high tolerance was obtained in persons of all ages to repeated and increasing injections of tetanus anatoxin. These inoculations were followed by the development of a strong specific active immunity. Tetanus immunization has become widespread in the military and civil populations in France during the past years. By July 1939 more than 1,500,000 persons had been immunized with tetanus anatoxin. Its use has been strongly advocated in the civil population and applied to children, mostly in a combined form, such as antitetanus-diphtheria or antitetanus-typhoid immunization. Compulsory antitetanus immunization was introduced in the French army by act of Parliament in 1936. The procedure necessitates three injections of tetanus-diphtheria-typhoid 2 cc. at intervals of three weeks. From 1936 until the outbreak of the war more than 800,000 men of the land, sea and air forces have been submitted to this combined prophylactic immunization and more than 75 per cent of them have already received the later reinforcing or "boosting" dose. The same measures have been extended to the French cavalry, and during the last three years more than 50,000 horses have been immunized. In England tetanus immunization was introduced in 1938 on a non-compulsory basis in the British army. At the outbreak of the war about 70 per cent of the men of the regular army had been immunized. Since the beginning of hostilities, immunization has been considerably extended. The same policy has been adopted in the Australian and Canadian expeditionary forces. In South Africa its application has remained limited either to immunization of individuals or of small communities especially exposed to the risks of tetanus infection; for example government, military, mining and health authorities, both in the Union and in several British African colonies, have used the procedure. The authors immunized children, using tetanus anatoxin mixed with diphtheria anatoxin or typhoid endotoxoid. Experience gained from several years of large scale immunization with this vaccine of half a million persons in the Union and elsewhere has shown that inoculation with typhoid endotoxoid is followed by a high antityphoid protection, accompanied by an exceptionally low incidence of reactions, as compared with TAB vaccine. Longer intervals are necessary for the development of antitetanus immunity in man as compared with typhoid. Mixed vaccine so prepared as to contain three parts of tetanus anatoxin and one part of typhoid endotoxoid of a high antigenic concentration was found to be practical. Three subcutaneous injections of the combined antitetanus-typhoid vaccine of respectively 1, 2 and 2 cc. were given at intervals of three weeks between the first and second inoculation and from seven to ten days between the second and third inoculation. The injection of the combined vaccine was followed by no more reactions than if the respective vaccines were inoculated separately. Serologic investigations on the concentration of tetanus antitoxin in the serum of immunized subjects seem to compare favorably with the results obtained by other investigators. The antityphoid agglutinins in the blood of some subjects after injection with combined tetanus-typhoid endotoxoid vaccine averaged above 1 in 1,000 for H and 1 in 100 for O agglutinins. Antitetanus immunization is indicated for all persons dealing with horses and agriculture, children because of their carelessness and soldiers under war conditions. Active immunization is the only means of conferring permanent protection under war conditions. This does not mean that serum prophylaxis is to be excluded. The two methods of active and passive immunity may be combined in some instances with benefit as a prophylactic urgency measure in nonimmunized wounded subjects.

Chinese Medical Journal, Peiping

57:301-400 (April) 1940

Transfusion Syphilis with Widespread Osteomyelitis and Cutaneous Lesions of an Erythema Multiforme Type. H. C. Pian and C. N. Frazier.—p. 301.

Cerebral Cysticercosis and Acute Poliomyelo-Encephalitis. Y. K. Hsü.—p. 318.

Phage Typing of Bacillus Typhosus and Its Epidemiologic Significance. C. H. Yen.—p. 330.

Schistosomiasis in Talifu Region of Yunnan Province. R. C. Robertson.—p. 358.

Epidemiology of Kala-Azar in China. R. Hoeppli.—p. 364.

Selections from Old Chinese Medical Literature on Various Subjects of Helminthologic Interest. R. Hoeppli and I. H. Ch'iang.—p. 373.

Schweizerische medizinische Wochenschrift, Basel

70:537-576 (June 15) 1940. **Partial Index**

Antihemorrhagic Vitamin K. P. Karrer.—p. 537.
Syphilis Fever Simulating Other Acute Infectious Diseases. A. Lemierre.—p. 549.
Parenteral Liver Extracts. W. Löffler and F. Koller.—p. 551.
"Insulitis" in Diabetes. H. von Meyenburg.—p. 554.
*Carotid Sinus Syndrome: Central Type. P. H. Rossier, M. Dressler and R. Simmen.—p. 563.
Acute Erythremic Myelosis: Case. O. Roth.—p. 571.

Carotid Sinus Syndrome (Cerebral Type).—Rossier and his associates discuss the etiology, symptomatology, diagnosis and therapy of carotid sinus disease in connection with four selected cases involving the cerebral type syndrome. The age of the patients was between 53 and 69 years. The features almost consistently present in the clinical picture of the case material studied were sudden attacks of dizziness accompanied with headache and a sensation of scintillation. Other symptoms, varying with the individual, were sudden facial skin discoloration, noise in the head or ears, cardiac pains, palpitation of the heart, dyspnea, loss of consciousness, vertigo on brusk movement of the head, temporary paresis of the arm and leg, a bad taste in the mouth and so on. Frequent signs accompanying the cerebral type syndrome included general illness, cardiac degeneration, digitalis intoxication and neuroses. In three of the four cases aortic sclerosis was roentgenologically discovered. Cardiographically recorded diagnostic tests by means of unilateral and bilateral pressure on the carotid sinus induced the pathologic phenomena of dizziness, mental confusion, loss of consciousness and clonic spasms with even greater intensity than appeared in the spontaneous attacks. Electrocardiograms were made with and without the use of atropine. The authors dwell on the physiopathologic mechanism of carotid sinus syndromes and the differential diagnosis between them and epilepsy. They state that carotid sinus involvements seem to occur with relative frequency but are not properly diagnosed. Carotid sinus pressure tests, simple in themselves, need to be made with all possible safeguards so as not to provoke unconsciousness, spasms or physical injury and be controlled by blood pressure and electrocardiographic checks. Syndromes of the cerebral type do not yield as readily to treatment as do the vagal type (atropine) and the vasomotor type, which can be managed by ephedrine. However, phenobarbital may be tried. All three types respond to anesthetization of the sinus. Roentgen treatments should precede attempts at surgical denervation of the sinus. Further investigations are necessary for the clarification of intracerebral pathologic conditions and of the regulatory processes that seem to inhere in the carotid sinus and gland areas.

Settimana Medica, Palermo

28:317-342 (March 30) 1940

*Behavior of Antistaphylococcus Immunity from Toxoid. P. Ritossa and G. Polistina.—p. 317.
Presence of Syncytium in Anterior Lobe of Hypophysis in Relation to Positive Results of Biologic Hormonal Tests in Pregnancy. N. Candela.—p. 328.

Antistaphylococcus Immunity from Toxoid.—Ritossa and Polistina made quantitative determinations of the staphylococcus antitoxins in the serum of nineteen patients with acute and subacute cutaneous staphylococcic infection, and of six normal persons previous to, in the course of, and after the administration of toxoid therapy. The toxoid used had an antigenic value which corresponded to sixteen staphylococcus units for each cubic centimeter of the preparation. The treatment was administered in six subcutaneous injections at intervals of four days and with progressive doses of 0.1, 0.25, 1, 1.5 and 2 cc. of the toxoid, up to a total dose of 5 cc. The amount of staphylococcus antitoxin in the blood serum of the patients before administration of the treatment varied from 1 to 5 antitoxic units per cubic centimeter of blood serum. There was an increase in the number of antitoxins in the blood serum of the patients and the normal persons, greater in the former than in the latter. In the patients it was progressive and paralleled the general improvement up to complete recovery. The increase of antitoxin in the blood serum from administration of toxoid was slow and scanty in two patients with diabetes and staphylococcic infection of long duration. The toxoid therapy exhibited a moderate antibacterial effect manifested by a moderate increase in the amount of agglutinins. The authors concluded that staphylococcus toxoid administered in the course of a cutaneous staphylococcic infection acts by producing antitoxic immunity, which is responsible for the therapeutic results.

Archivos de Pediatria del Uruguay, Montevideo

11:177-432 (April) 1940. **Partial Index**

*Blood Transfusion in Bronchopneumonia of Children. M. Acuña.—p. 197.
X-Ray Examination of Lung in 100 Cases of Tuberculous Meningitis in Children. J. Bonaba and J. A. Soto.—p. 391.

Blood Transfusion in Bronchopneumonia of Children.—Acuña resorted to blood transfusions in bronchopneumonia of a large number of nurslings and young children treated in the pediatric clinic of Buenos Aires. He prefers fresh citrated blood whenever available. Otherwise blood which has been preserved for not more than from two to five days can be used. Blood from convalescents or from persons who had had bronchopneumonia is preferred. The amount of blood to be transfused must not exceed an average of 15 cc. of blood for each kilogram of body weight. The transfusion is done slowly by the gravity method. When the fontanels are open the blood may be infused into the upper longitudinal sinus by gravity at the rate of from 3 to 5 cc. a minute. In grave bronchopneumonia with a tendency to collapse or to signs of cardiac failure, transfusion should be preceded by the withdrawal of from 20 to 50 cc. of blood from the patient. Transfusion is best given early in the course of the disease. It is given every other day in acute cases and at intervals of three days in subacute and mild cases up to a total of five or six transfusions with blood from different proper donors to prevent shock. Hygienic, dietetic and symptomatic therapy is likewise carried out as indicated. There are no contraindications to early transfusions in infants and in young children. Blood transfusions seem to exert a favorable effect on the course of bronchopneumonia by producing immediate relief in the respiratory and nervous symptoms and improving the general condition of the patients. Of the patients thus treated, 70 per cent recovered.

Medizinische Welt, Berlin

14:545-572 (June 1) 1940. **Partial Index**

Wound Diphtheria: Its Clinical Aspects, Treatment and Prophylaxis. M. Gundel and W. Heine.—p. 545.
*Acute Articular Rheumatism. F. Gudzent.—p. 547.
Significance of Roentgenoscopy for Diagnosis and Differential Diagnosis of Acute Abdominal Disturbances. H. Bade.—p. 551.
Practical Results of Research on Venereal Lymphogranuloma. A. Boldt.—p. 554.
Calcium in Therapy of Heart Disease. A. Merten.—p. 556.
Dry Blood Test in Mass Examinations in Campaign Against Syphilis. P. Dahr.—p. 557.

Acute Articular Rheumatism.—Acute articular rheumatism is widely regarded as an infectious process. The theory is based chiefly on the clinical course with its acute onset, fever and inflammation of the joints. According to Gudzent several factors contradict the infectious origin: the failure to detect a specific organism of acute articular rheumatism and the facts that the disease has never been transmitted by contact, that no micro-organisms have ever been found in the inflammatory foci of rheumatism and that it has not been possible to produce articular rheumatism in animals by means of infectious organisms. Acute articular rheumatism is occasionally preceded by a tonsillitis, but the percentage of such cases is too small to justify citing tonsillitis as proof of the infectious character of rheumatism. Many investigators regard foci of infection as the cause, but studies on the efficacy of tonsillectomy in preventing relapses of acute articular rheumatism disclosed that recurrences were about as frequent in those having undergone tonsillectomy as in those who had not. It appears that the theory of the infectious origin of rheumatism has not been definitely established. The author was able to produce rheumatic tissue lesions in animals by means of various types of proteins. Observations on patients indicated that food proteins (animal, as well as

vegetable) are chiefly responsible. They produce under certain conditions antibody-antigen or allergic reactions with their cytotoxic effects on the connective tissue and thus develop rheumatic tissue lesions. An allergic tendency is, however, a necessary requirement for this harmful action. The family histories of the author's patients nearly always revealed allergic diseases among their blood relatives. The allergic tendency of patients with rheumatism is hereditary but their specific protein allergy is acquired. The author admits that there are other contributary factors such as colds, overexertion and endocrine influences. The importance of the latter factor is proved by the frequent development of acute articular rheumatism during adolescence and in connection with thyrotoxicosis. The author stresses rest in bed and careful nursing as the first requirement in treatment. These measures alone effect a cure in some cases. Other measures consist in restriction of the protein intake, search for the offensive allergen and its elimination from the diet. The low protein diet should be continued until cure has been established. Desensitization with the offensive allergen should be instituted if possible. Medicinal treatment with salicylic acid, aminopyrine and cinchophen should not be neglected. The author maintains that these medicaments have an antiallergic rather than an antiinfectious action. He gives intravenous or intramuscular injections of calcium or strontium preparations, because they also exert an antiallergic effect. Massage and gymnastic exercises are recommended for the cases with residual stiffness or ankylosis.

Zeitschrift für Tuberkulose, Leipzig

84:313-388 (May) 1940.

Copper Therapy in Pulmonary Tuberculosis. G. Goralewski.—p. 313.
Use of Fluorescence Microscopy in Detection of Tubercle Bacilli. P.-P. Schneider.—p. 319.
*Evaluation of Gold Therapy in Pulmonary Tuberculosis. P. Martini and A. Rosendahl.—p. 330.
Economic Aspects of Persons with Open Tuberculosis. R. Steinwegs. —p. 340.

Gold Therapy in Pulmonary Tuberculosis.—Martini and Rosendahl examined 140 of the 150 contributions to the subject of sanocrysin therapy in pulmonary tuberculosis. They found that only eight authors conformed to the critical standards required for the scientific evaluation of a new therapy (Moellgard's sodium aurothiosulfate, 37 per cent gold, dates from 1924), such as pretherapeutic observations, careful making of protocols during the course, absence of simultaneous use of other medication, size of case material, length of therapeutic management, full laboratory tests and records. These eight authors arrived at negative results stated in terms of failures, deaths and toxic secondary effects. Toxic sequels such as high fever, shock, pain in the joints, cutaneous phenomena, gastrointestinal disorders, kidney lesions (with nine deaths), albuminuria and other renal complications were reported by eighty-four authors, sixty-six of whom favored the use of sanocrysin. Toxic effects were not confined to records of high dosage but observed also by authors who had employed low and moderate doses.

Geneeskundig Tijdschr. v. Nederl.-Indië, Batavia

80:1181-1244 (May 7) 1940

*Bromide Intoxication. P. M. van Wulfften Palthe.—p. 1182.
Ophthalmologic Studies on Population of Groot Atjeh (Sumatra) During 1937. C. E. Gomperts.—p. 1192.
Eczematous, Impetiginous and Ulcerous Diphtheria of the Skin. D. P. R. Keizer.—p. 1239.

Bromide Intoxication.—Van Wulfften Palthe relates the history of a man, aged 40, with symptoms resembling those observed in acute alcoholic hallucinosis and in delirium tremens. There was severe motor unrest, perplexity, confabulation, hallucinations, hypersuggestibility, disorientation, intermittent loss of consciousness, tremors and mild increase in temperature. There was no history of alcoholism, but inquiry revealed that the patient had taken large quantities of bromides, at first on medical prescription and later on his own initiative. During the last three months he had taken 25 Gm. a week. On the assumption that the psychosis of this patient might be the result of bromide intoxication, the different body fluids were examined for the presence of bromide. The determinations were made according to the method of Ulrich. It was found that, as the bromide content of the body fluids decreased, the psychic state of the patient improved. The author directs attention to Gundry's report in THE JOURNAL, Aug. 5, 1939, page 466. He cites another case of his own. Cessation of the bromides is the first step in the therapy. The elimination of bromides can be accelerated by the administration of sodium chloride, the chlorine driving the bromine out of the cells. Large quantities of sodium chloride, however, are dangerous. The safest method, that which he employed in his two cases, consists of a normal diet and generous quantities of fluid. Scopolamine is helpful in counteracting severe psychic symptoms. The author concludes that, although caution is advisable in the administration of bromides, it is not necessary to discontinue the use of valuable medicaments. Bromide intoxication is relatively rare. Apparently, several factors are necessary to produce it.

Nordisk Medicin, Gothenburg

6:893-922 (May 11) 1940. **Partial Index**

Hygiea

*Arterial Anemia in Children. B. Hamne.—p. 905.
Has Active Treatment of Fractures of Heel Bone in Recent Years Affected Invalidity? Experience in 412 Cases with State Insurance. T. Olovson.—p. 911.

Arterial Anemia in Children.—Hamne states that the circulatory disturbance described by Bjure and Laurell in older adolescents is not unusual in younger children and reports eleven cases of arterial anemia in children aged from 7 to 12. The symptoms include abnormal physical and psychic fatigue, a feeling of bearing-down pressure on the head and headache, backache, diffuse gastric discomfort, palpitation of the heart and often orthostatic albuminuria, not all present in all cases. The disorder occurs in tall, thin persons from long standing or sitting and is due to abnormal displacement of blood from the upper to the lower parts of the body because of these postures. When the patient stands the diaphragm falls and the heart becomes drop shaped, decreasing abnormally in volume. In the cases described there was an average pulse increase of 27 beats a minute with simultaneous decrease in pulse pressure, which in two of the cases fell to 15 mm. of mercury. In two cases the x-rays revealed a so-called drop heart. Orthostatic albuminuria was seen in five cases. The author believes that there is a relation between arterial anemia and disposition to pulmonary tuberculosis. He emphasizes the importance of attention on the part of school physicians and teachers to these children, often backward in school, and says that the disturbance disappears if the patient gains in weight and the abdominal muscles are strengthened. A balanced diet is recommended, with the principal meal immediately after school and followed by an hour's rest in the horizontal position. An abdominal support is helpful and exercise of the abdominal muscles is called for.

6:985-1016 (June 1) 1940. **Partial Index**

Norsk Magasin for Lægevidenskapen

*Prognosis in Epidemic Encephalitis. H. J. Ustvedt.—p. 997.
Lipomas in Intestinal Tract. C. Bruusgaard.—p. 1002.

Prognosis in Epidemic Encephalitis.—Ustvedt says that, of the 107 patients with epidemic encephalitis treated from 1919 to 1934 by Economo, 16 per cent died in the acute stage. Of the surviving ninety, eighty-seven were followed for from one to nineteen years, fifteen of them for from fifteen to nineteen years. Thirty were fully capable of work and without symptoms, ten were capable of work but had slight symptoms possibly attributable to the encephalitis, and twenty were capable of work but had certain symptoms, in some cases troublesome. In all, sixty were able to work. Of the twenty with chronic encephalitis, eleven died. The longest interval between the acute stage and new symptoms was eight years. The author says that there are far fewer cases of epidemic encephalitis in Norway than in most European countries and that the immediate mortality seems to have been moderate and after-examination with respect to ability to work shows conditions far more favorable than might be expected.